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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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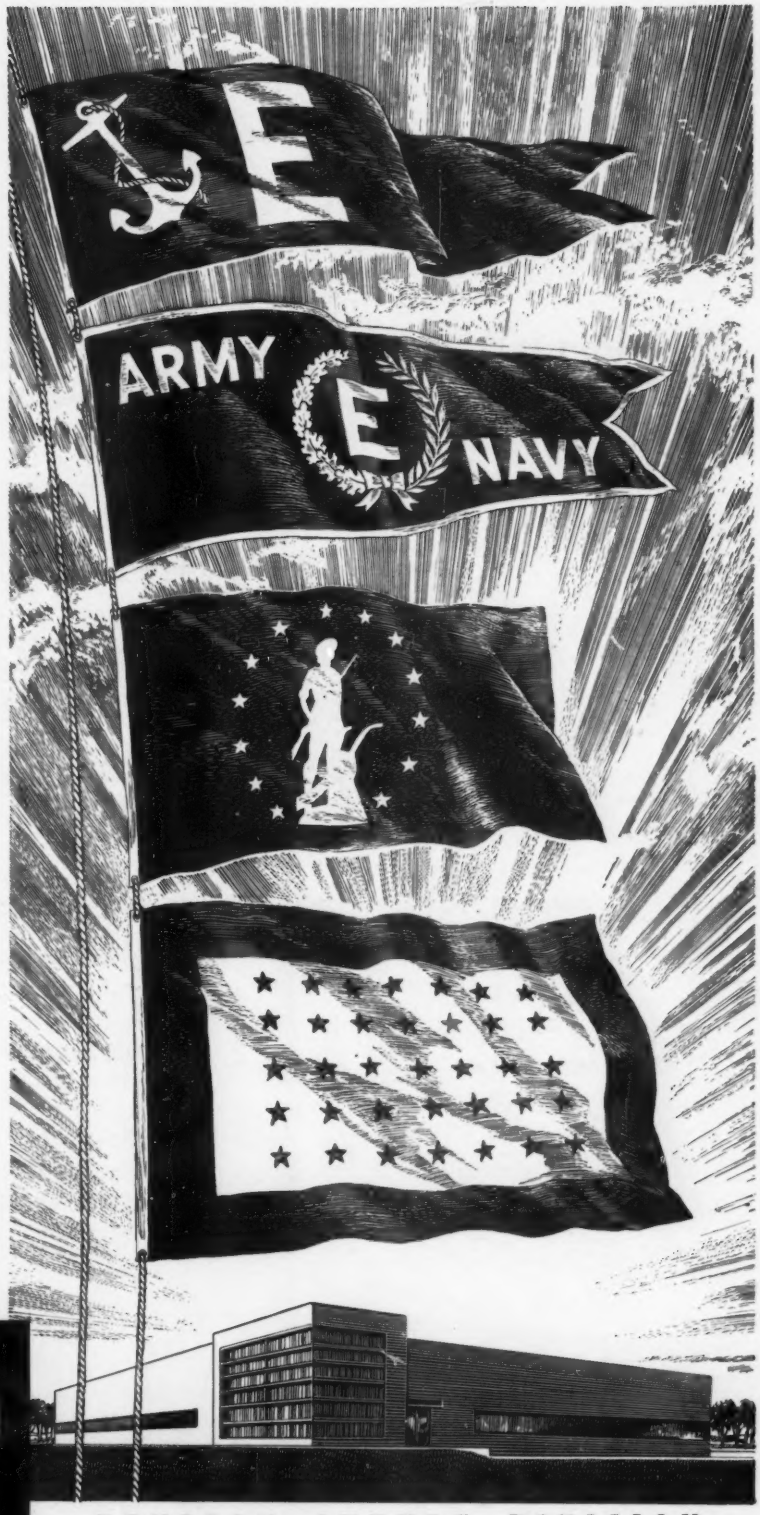

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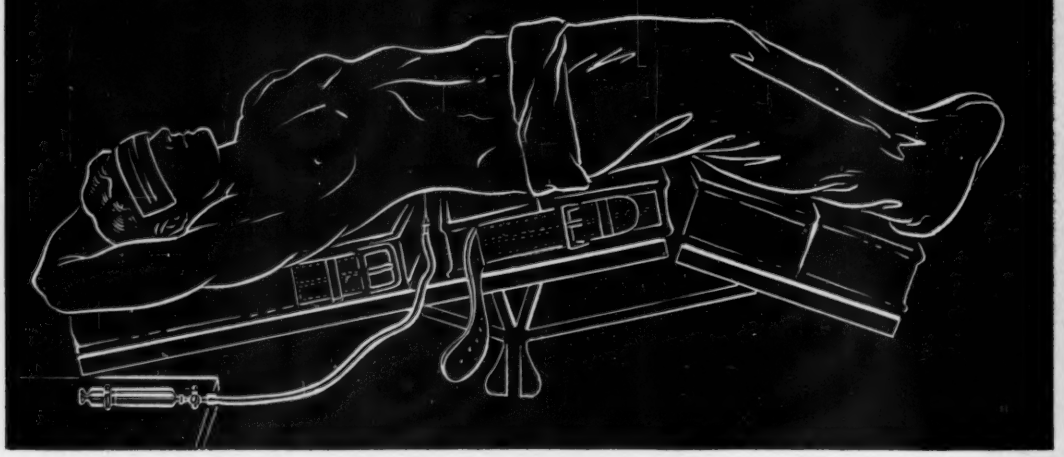

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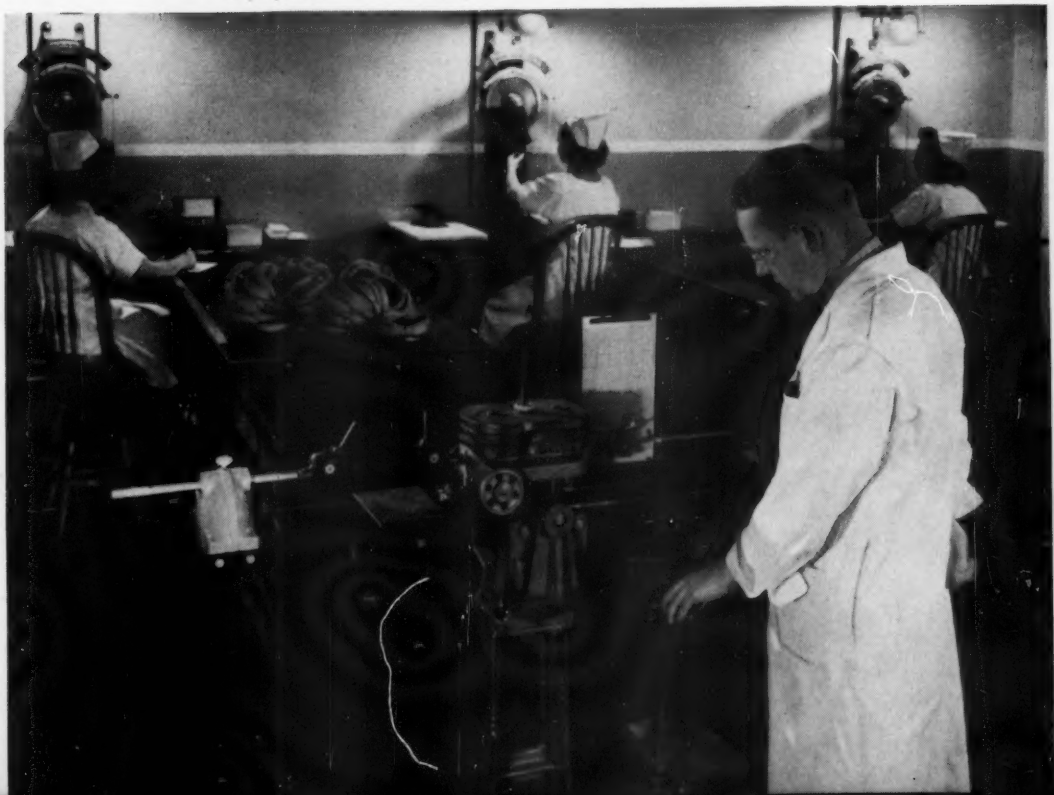

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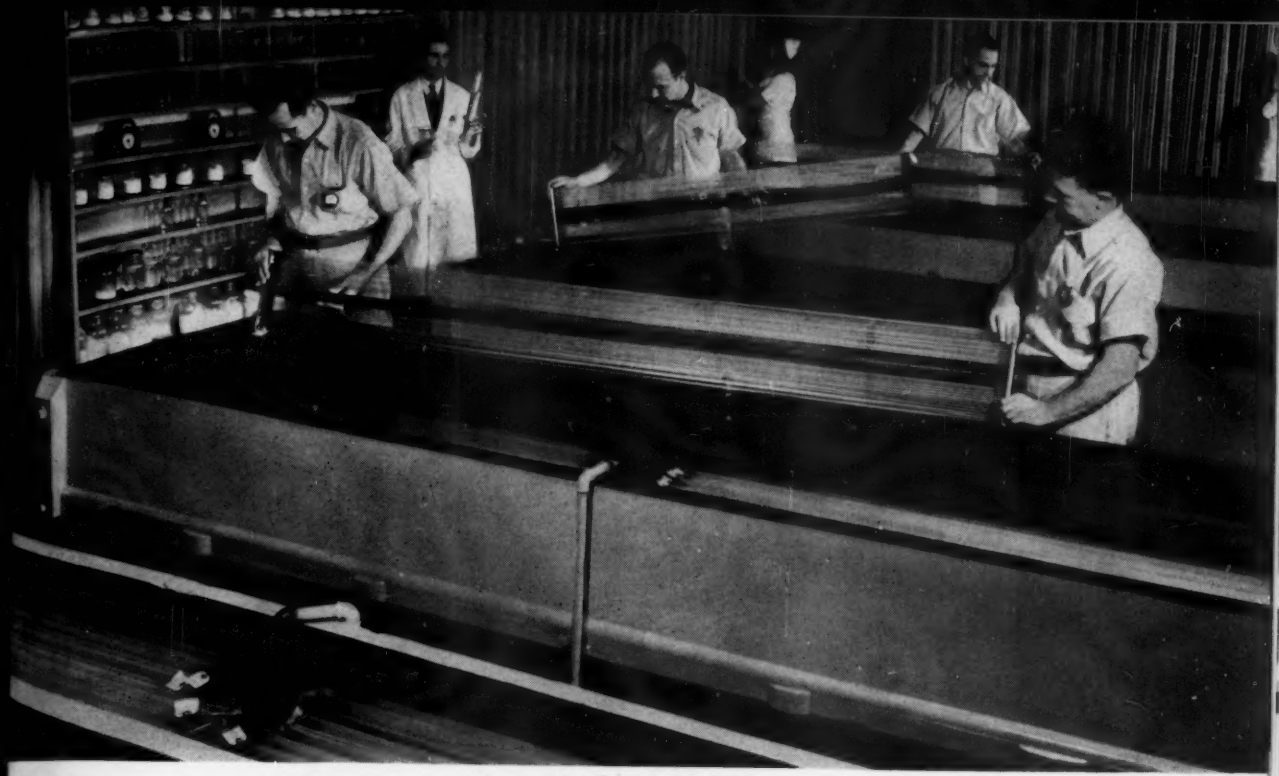

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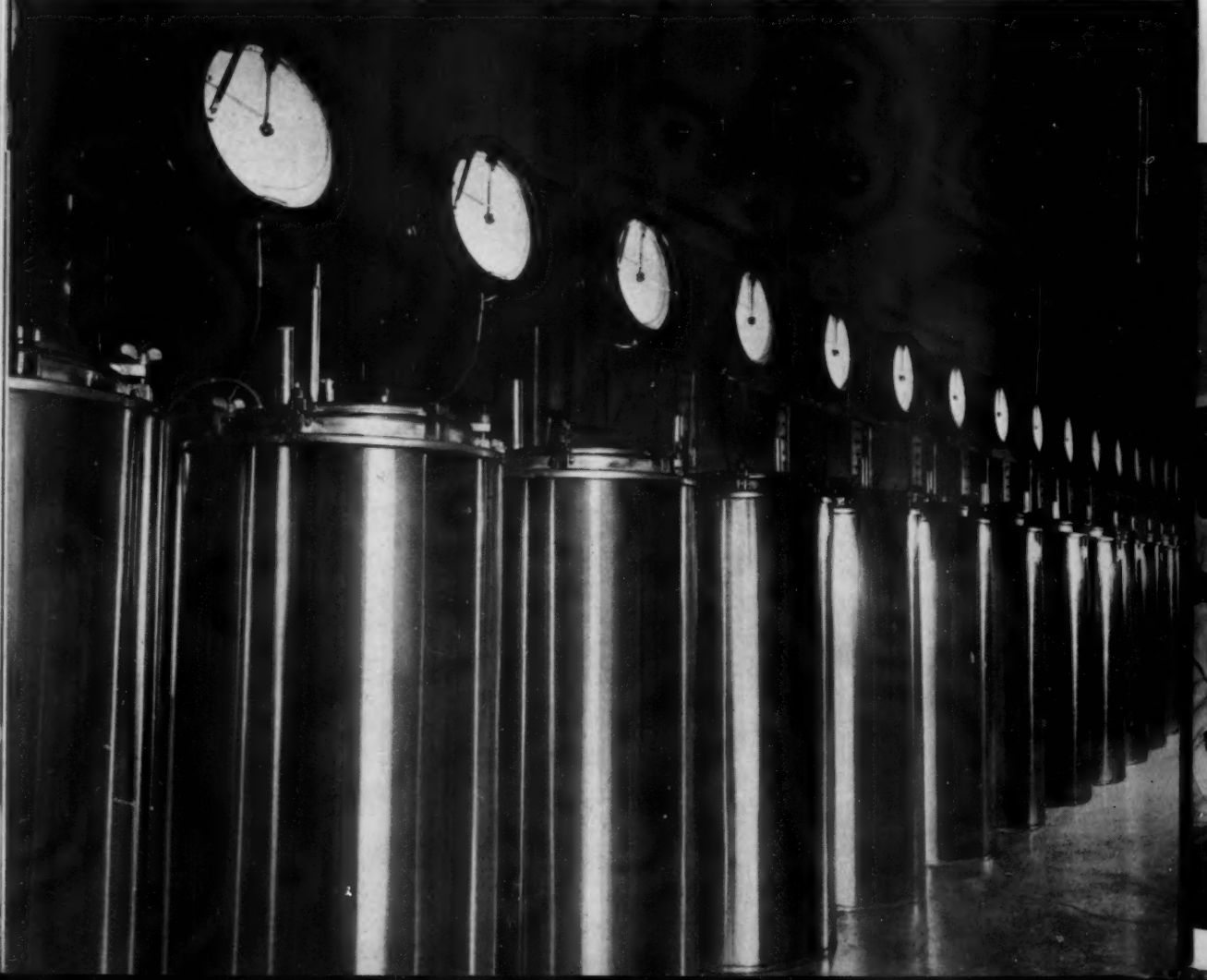

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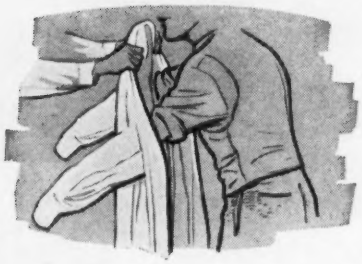

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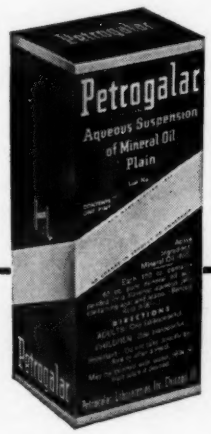

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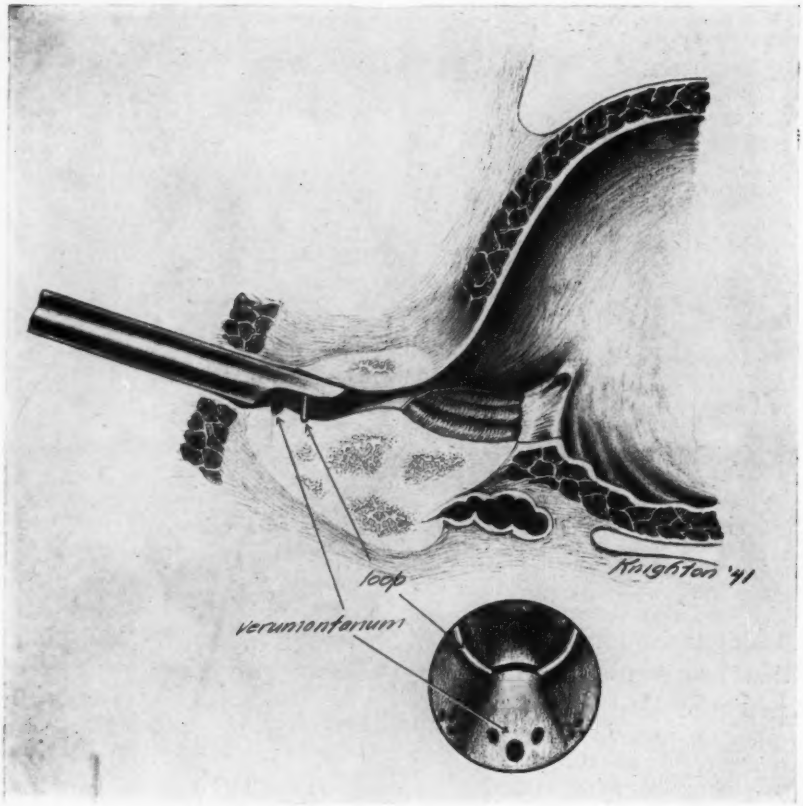

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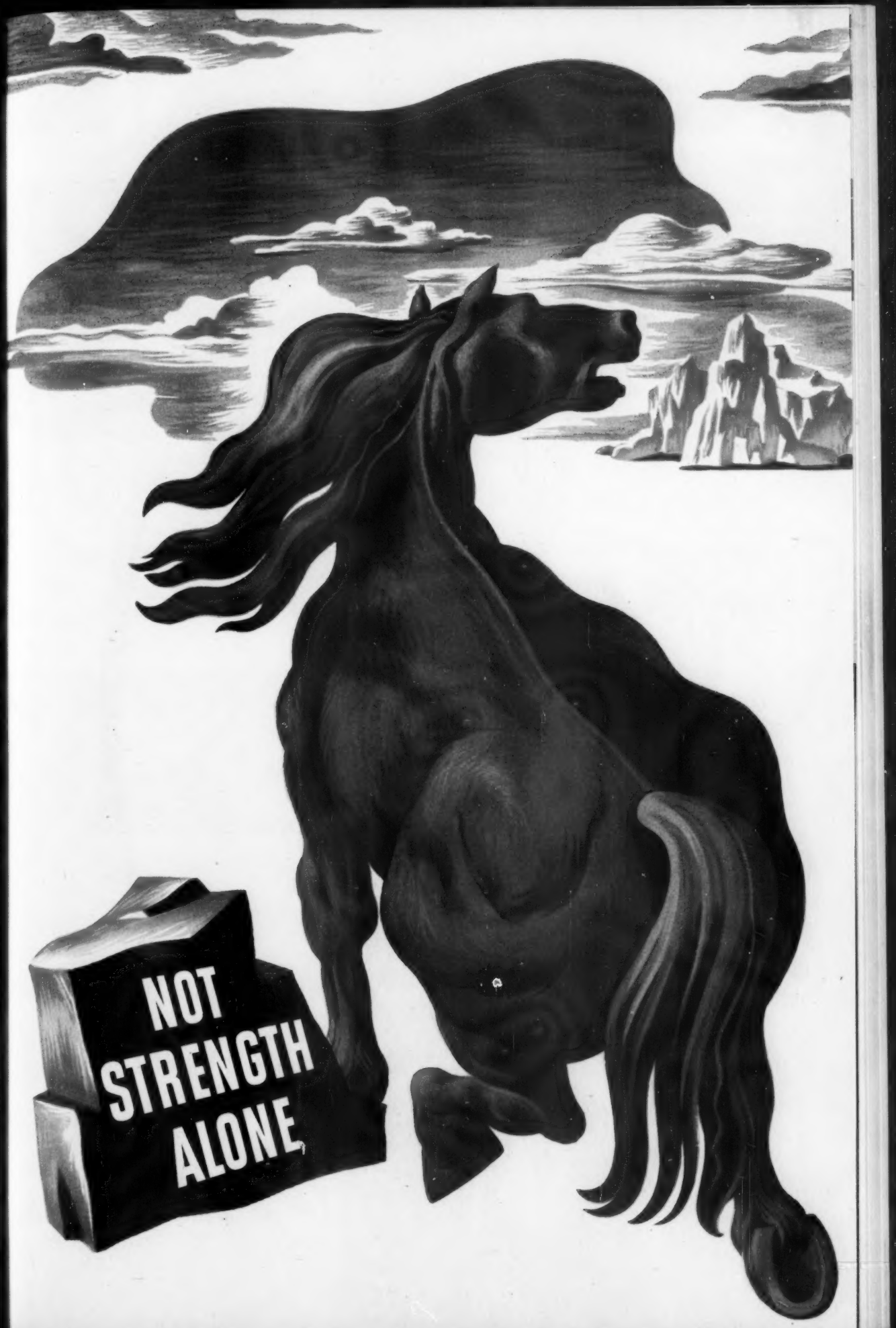
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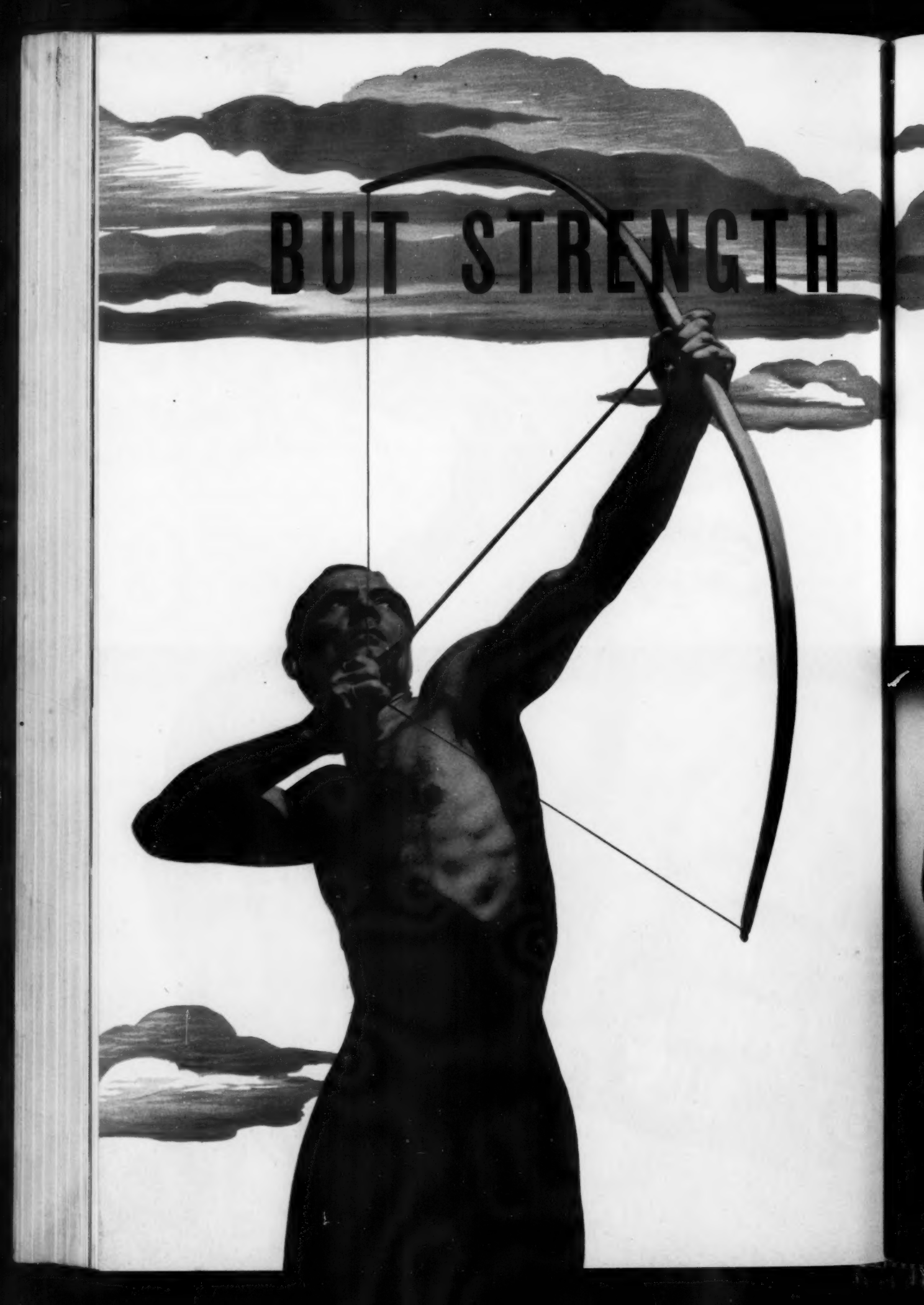
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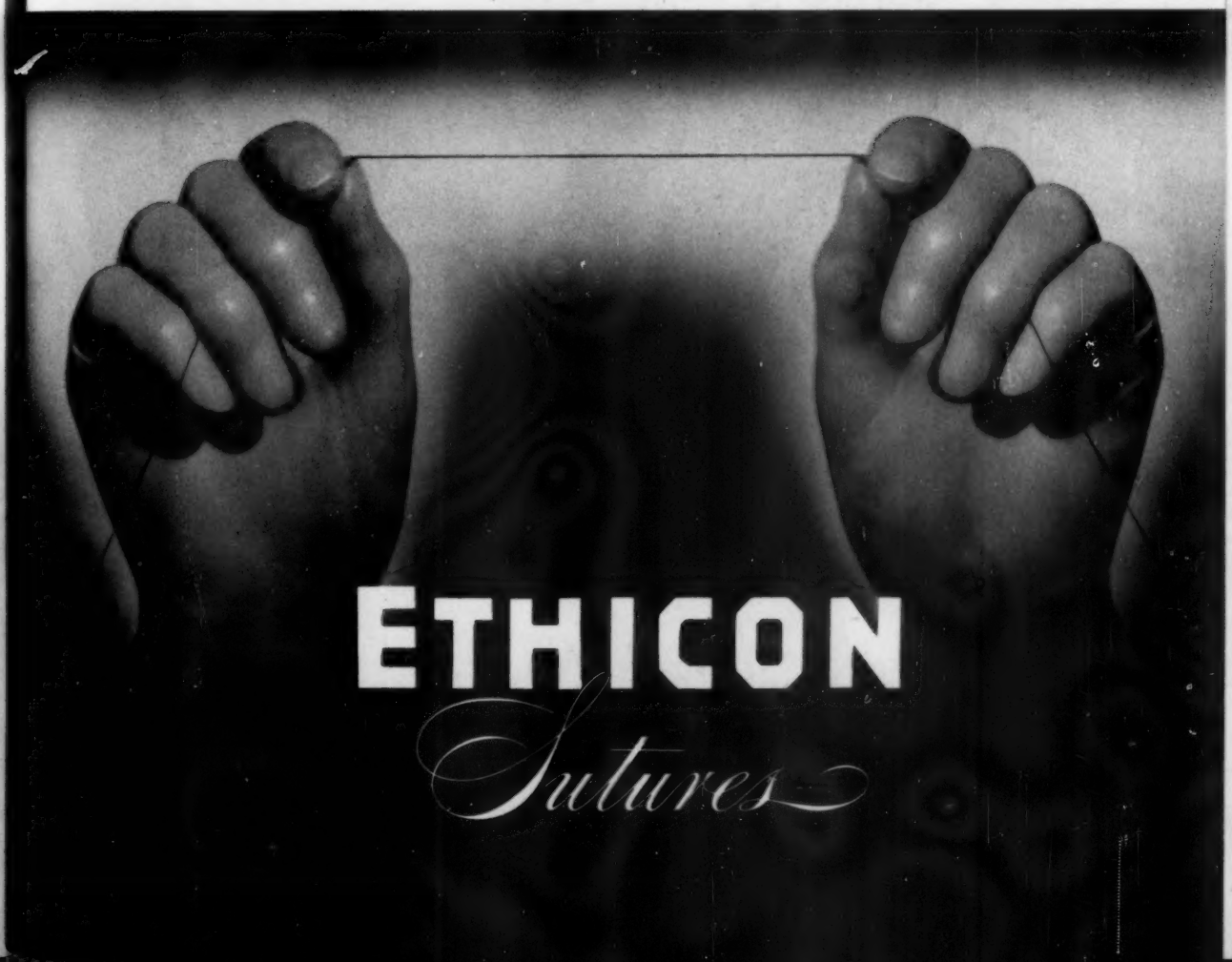

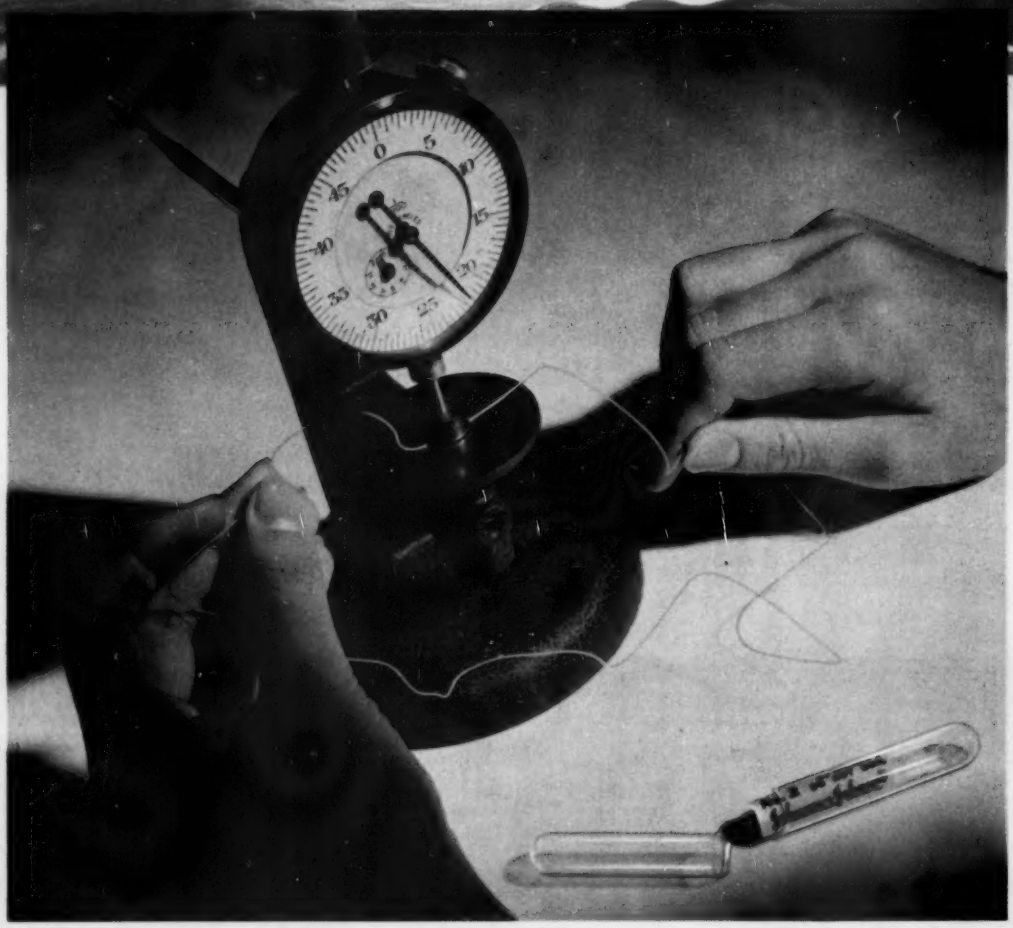

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VOL. 13 FEBRUARY, 1943 NO. 2

Original Communications

SURGERY OF THE SPLEEN IN BLOOD DYSCRASIAS

E. L. ELIASON, M.D., AND L. W. STEVENS, M.D., PHILADELPHIA, PA.

(From Surgical Service A in the Medical School and Hospital of the University of Pennsylvania)

IT IS our purpose to limit the scope of this presentation to the blood dyscrasias that are favorably affected by surgical procedures directed on the spleen, i.e., splenectomy, or indirectly upon its blood supply by ligation of its vessels. Justification of these procedures must be evaluated by the mortality and the morbidity following such treatments. Splenic surgery has been employed sporadically since before Christ and, later on, occasionally and specifically for the purpuras, splenic anemias, and the ictero-anemias with fairly good results. The field, however, was broadened disastrously when pernicious anemia, leucemia, aplastic anemia, toxic infections, allergies, drug anemias, etc., were included. Such injudicious surgery produced either a high mortality or left the surviving patient usually worse for the experience. In the last twenty to twenty-five years, with a more rational selection of cases and improved pre- and post-operative care, splenectomy has earned a foremost place in the treatment of splenic anemia, idiopathic or essential thrombocytopenic purpura, and hemolytic ictero-anemia. An attempt will be made, therefore, to present the facts and evaluate surgery on patients suffering from one or the other of these three conditions.

SPLENIC ANEMIA

Osler defined this condition as "an intoxication of unknown origin characterized by great chronicity; progressive enlargement of the spleen which cannot be correlated with any known cause, anemia of the secondary type with leucopenia, a marked tendency to hemorrhage, particularly from the stomach (esophagus), and in many cases a terminal state with cirrhosis and jaundice." Much work has been done in this field since then (1900), and yet we are, after extensive work by the pathologist and hematologist, still in the dark concerning the etiology. This ignorance of etiology is an important point in diagnosing the pa-

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tient with the above pathologic and physical findings. In other words, the diagnosis today continues to be one of exclusion before surgery should be practiced. The Banti's syndrome with a known etiologic factor justifies medical and not surgical treatment.

In the last ten years writers have attempted to explain this picture in various ways. Thompson, from the Spleen Clinic at the Presbyterian Hospital, New York City, on a series of sixty-eight splenectomies for this condition, draws the following conclusions: (1) It results from a variety of lesions that produce a hypertension in the splenic vein; (2) it is purely a mechanical congestion; (3) cirrhosis of the liver is only one obstructive cause which, if not existent at the time of splenectomy, will not develop subsequently; (4) suggests we designate the syndrome as a congestive splenomegaly in place of the old term Banti's disease. Drenckhahn is inclined to think that if the viscosity of the blood in these cases is lowered by venesections, the hemorrhages will be less frequent and less massive. Whipple, in 1937, reported thirty-one cases of Banti's disease with fifteen of unknown etiology. He felt then that portal hypertension was the factor to investigate. One of us (E. L. E.) found twenty splenomegalies in patients with anemia at the Philadelphia General Hospital in the last five years, two of which were diagnosed splenic anemia (Banti) and eighteen of which were classed as of undetermined origin. Davidson (1934) showed that the blood picture was not reliable, stating that the red blood corpuscles and hemoglobin can be restored to normal with iron.

Treatment.—Howells reports ninety-four cases and compares the medical and surgical results (Table III). Splenectomy in fifty-one patients gave improvement in 43 per cent; medical care of forty-three patients gave 46 per cent improvement. He further found that in both types a hemoglobin of 60 per cent + accompanied improvement in an average of 59 per cent, whereas if the hemoglobin was between 30 and 60 per cent, the average improvement in both instances was only 33 per cent. His conclusions were that splenectomy does not improve the expectancy of life nor prevent the progress of the cirrhosis or the anemia or the recurrence of hematemesis. Therefore, "it is illogical to retain it as a routine method of treatment." Again, of thirty-one patients, Whipple (1937) had eighteen live, one as long as eleven years. His experience was that of the patients who had preoperative hemorrhages, eleven in number, seven died from hemorrhage. His conclusion was that splenectomy increases life expectancy but does not alter the condition of patients with hemorrhage and is not advisable in severe anemias. Wada (1941) states that in his series of seventeen cases of Banti's disease, the operative mortality in patients with early cases was nil, whereas in patients with the delayed cases it was 40 per cent. Pemberton, in 1931, in a series of 167 cases, found that ninety-eight of the patients had history of preoperative hematemesis; twenty-nine of these, or 29 per cent, died from hematemesis and only nine from thrombosis. He also found one patient

lived nineteen years and ten lived over nine years. This same clinic found that 50 per cent of their patients bled before operation and also after operation. Whipple, quoted by Rives, has now 107 splenectomies to his credit, fifty-six of which were for splenic anemia. Ranzi, in 1936, reported twenty-one cases. Of the fifteen patients followed, one was well after twenty years, two were not benefited, and seven were well from two months to two years. Evans states that one-half of his patients had recurrence of hematemesis, with several deaths.

Eliason and Johnson, in 1937, reported cases of twenty-one patients. Seven of the deaths were directly due to liver damage, three of these had hemorrhage; of the survivors, one lived eleven years, two lived seven years, two lived five years, two lived three years, etc.

Diamond, in 1938, reported eight cases in children diagnosed as splenic anemia, by reason of splenomegaly of unknown origin, chronic progressive hypochromic anemia, a constant leucopenia, and thrombocytopenia. Splenectomy was followed by a rapid rise in the leucocytes, an elevation of the platelet level, and a permanent improvement in the anemia. Six of the eight have remained well for from six to ten years, with no evidence whatever of the disease. These results can be viewed with great satisfaction.

Pemberton (1940) reports on splenectomy in 215 patients with splenic anemia and Banti's syndrome with a hospital mortality of 9.8 per cent but with a most gratifying life expectancy record: 54.6 per cent lived five years +; 41.5 per cent lived ten years +; and 20.4 per cent lived twenty years or more. His experience is that 50 per cent of patients with hemorrhage before operation also bled subsequently despite the employment of one or more of the indirect methods of vessel ligations or omentopexy.

Rousselot (1938) from the Spleen Clinic in the Presbyterian Hospital, New York City, reports fifty-five patients with Banti's syndrome which condition is termed congestive splenomegaly, therein including Laennec cirrhosis, 14 with 4 deaths; cirrhosis unclassified, 2 with no deaths; schistosomiasis, 11 with no deaths; and obstructive factor undetermined, 13 with 3 deaths; also cirrhosis unclassified and thrombosis, 3; portal vein transformation, 2; and stenosis of portal vein, all with no deaths. Further statistics will appear in the Tables I, II, III, and IV.

In our series of twenty-eight patients treated by splenectomy, there was a mortality of 25 per cent; 28 per cent of the survivors lived five years and 21 per cent lived ten years.

It is to be noted from a study of Table IV that the mortality figures ranged from 0 to 40 per cent. This would seem to indicate that some factors, probably the degree of cirrhosis and liver damages, varied greatly. This was the case in our series, seven of the eight patients who died having extensive damage to the liver.

Ligation of coronary vein, splenic vein, artery or pedicle, and injection of esophageal varices have been done in a few cases only and with

TABLE I

SPLENIC ANEMIA (BANTI)

CONGESTIVE SPLENOMEGALY

AUTHORS	SPLENECTOMY	HEMORRHAGE	
		PREOP. (%)	POSTOP. (%)
Thompson	68	40	59
Whipple (1931)	31	73	63
Pemberton (1931)	167	50	50
Pemberton (1940)	215	59	50
Rousellot (1939)	55	?	12
Diamond*	11	?	50
Evans	?	?	50
Eliason and Stevens (1942)	28	7	35

*Children.

TABLE II

SPLENIC ANEMIA

FOLLOW-UP DATA

AUTHORS	5 YR. (%)	10 YR. (%)	20 YR. (%)
Pemberton (1940)	55+	43+	22+
Ranzi (1936)	5+	5+	4+
Diamond (1938)	75	75	—
Rousellot (1939)	20	10+	—
Whipple (1937)	58+	58	
Eliason and Stevens (1942)	28+	21+	—

Eighty-nine per cent returned for follow-up.

TABLE III

SPLENIC ANEMIA MORBIDITY

MEDICINE VS. SURGERY

		HGB. %	AVERAGE IMPROVEMENT	% IMPROVEMENT
51 Surg. 43 Med.	Group I	60+	30 Surg.	43
			Med.	63
	Group II	30 to 60	33 Surg.	30
			Med.	39
	Group III	Below 30	31 Surg.	31
			Med.	33

TABLE IV

SPLENIC ANEMIA MORTALITY

AUTHORS	(%)
Pemberton	12.4
Ranzi	40
Diamond	25
Andrus and Holman	0
Rousellot	14.5
Eliason and Stevens	25

only indifferent results, which seems to show that persistence of varices after operation dooms the patient and nothing will correct them. Rhoads and Stein report a case in a child in which the varices were definitely reduced following the triple procedure of splenectomy and ligation of both the gastric artery and the coronary vein.

Conclusion.—Splenectomy gives the patient the best chance. The earlier in the disease that splenectomy is done, the lower the surgical mortality and the greater the life expectancy. It is the opinion of one of us (E. L. E.) that this is the only choice, even with cirrhosis. The operative mortality should not be over 10 per cent at the worst, and some of the patients have lived twenty years.

PURPURA HEMORRHAGICA

Under this heading the surgeon is concerned only with essential thrombocytopenic purpura, and for this reason it is important for our hematologists and medical colleagues to eliminate the innumerable other causes of purpura before advocating splenectomy. The concensus of opinion today is that the findings in the essential group are petechial hemorrhages and bleeding from the mucous membranes, low platelet count, prolonged bleeding time, normal coagulation time, delayed or absent clot retraction, a secondary anemia with evidence of regeneration, a normal or increased total white count with a normal differential count, a positive tourniquet test, and a spleen that may or may not be enlarged.

Errors in diagnosis are more frequently made in patients with leucemia and aplastic anemia with purpuric phenomena due to allergies, drugs, particularly sedormid, etc.

Essential purpura as it confronts the surgeon may be divided into four groups.

Group I: Mild or moderate bleeding in the initial attack. Conservatism and possibly transfusions are all that are necessary for a high per cent of permanent cures.

Group II: Mild bleeding with recurrent attacks. Here again there is almost uniform agreement that, conservatism failing, splenectomy is definitely indicated.

Group III: The fulminating type in the initial attack. Here we have the most difficult problem of all. Up to 1932, when a survey was made of the literature by Eliason and Johnson, in thirty-five patients the mortality was 34.3 per cent. In the next twenty-one patients reported up to 1936, the mortality was reduced to 13.6 per cent, and yet in 1936 Giffin reports a 50 per cent mortality and Whipple, in 1937, mentioned seven deaths in eight patients with fulminating cases. McLean and Amesse each report a high per cent of deaths. Rosenthal, in 1939, in an analysis of 153 cases, states that splenectomy is contraindicated in acute purpura in children, in acute purpura with fever and leucocytosis, and in megakaryophthisis. He found a high per cent of the patients with acute cases (thirty-eight) recovered spontaneously.

It is still difficult to evaluate the findings due to lack of data, but it is not unlikely that the high mortality has been due to delayed splenectomy and insufficient postoperative care. Possibly, due to greater knowledge on the part of our hematologists and the expansion of blood banks, the mortality of the last two or three years may prove to turn out much lower.

Group IV: Severe bleeding in recurring attacks. These patients having shown by their history that they have survived by reason of remissions should be treated accordingly by transfusions as long as they improve by this regime. However, should such not be the case, splenectomy is indicated at once.

The results following removal of the spleen for purpura hemorrhagica have been so satisfactory that when the disease is an inconvenience and has not responded to nonoperative treatment, a splenectomy should be advised. According to reports up to 1932 (Eliason and Ferguson), 87 per cent of 179 with follow-up reports were thus cured. Unfortunately, there was a woefully short follow-up in many instances. Pemberton, in 1934, with long follow-up periods, reported 63 per cent as permanently cured by ectomy. Giffin, back in 1927, stated that he has never seen purpura persist after splenectomy coupled with a conscientious elimination of foci of infection (Table V). Vaughan (1939) reports six patients all surviving from ten to fifteen and one-half years after splenectomy and states that "these six bring the total reported cases to fifty-nine patients living from five to fifteen and one-half years after operation." Diamond in his study of twenty-eight cases in children states that this disease tends to be more acute in children than in adults. Eight of these had a splenectomy performed after other measures had failed; six of these were completely relieved and have maintained normal platelet counts since then. Two were only moderately improved; of the twenty treated medically, twelve have had spontaneous and permanent remissions; six continue with occasional bleedings and permanent low platelet counts. Two died from intracranial hemorrhages. His advice is to advocate surgery only in the severe cases (Table VI).

Thomas (1927), with his sixty-two patients, reached the same conclusion.

TABLE V

PURPURA HEMORRHAGICA

FOLLOW-UP DATA

AUTHORS	5 YR. (%)	10 YR. (%)
Literature (1932)	87	
Pemberton (1934)	63	
Vaughan (1939)		6 cases
Pemberton (1940)	89	87
Rousellot (1938)	42	19
Eliason and Stevens (1942)	50	21

One hundred per cent returned for follow-up.

TABLE VI

FULMINATING PURPURA HEMORRHAGICA

AUTHORS	MORTALITY (%)
Literature (1932)	34.3
Literature (1936)	13.6
Giffin (1936)	50
Amese	High
Whipple (1937)	87
McLean (1937)	High
Diamond (1938)	25
Andrus and Holman (1939)	0
Eliason and Stevens	0

Pemberton (1940) performed splenectomy for purpura on eighty patients with hospital mortality of 8.8 per cent and a five-year survival of 89 per cent and a ten-year survival of 87 per cent. He, of course, adheres to his 1933 statement; namely, "In the treatment of purpura of mild severity, splenectomy is not recommended until other measures fail. Since in the acute forms the dangers of delay outweigh those of operation and since splenectomy is the surest cause of remissions, commonly complete and permanent, such should be the treatment." Elliott (1938) reports from the Spleen Clinic twenty-one patients with splenectomy for idiopathic purpura with no operative deaths and with nine known five-year cures and four ten- to eighteen-year cures. Eleven patients all operated upon less than five years are living and well. Expressed further, they found that splenectomy gave satisfactory results in 85.7 per cent, and conservative treatment of twenty other patients gave satisfactory results in only ten per cent of the cases (Table VII).

TABLE VII

PURPURA HEMORRHAGICA
SURGICAL MORTALITY

AUTHORS	NUMBER OF CASES	MORTALITY (%)
Diamond	8	0
Pemberton (1940)	80	8.8
Elliott (1938)	21	0
Eliason and Stevens (1942)	15	6.6(?)*

*(?)Only death, error in diagnosis.

Conclusion.—Mild purpura does not require splenectomy until other measures fail. Acute purpura should be treated by early splenectomy as the surest and safest course to pursue, both as to mortality and morbidity.

HEMOLYTIC JAUNDICE

Hemolytic jaundice, also termed ictero-anemia (acholuric jaundice) for many years, was classed as congenital or acquired. Of recent years, this differentiation has less and less followers, it being felt that they are one and the same. It does seem, however, to other clinicians that there is good reason to continue to differentiate them.

Hemolytic ictero-anemia is characterized by the finding of secondary anemia of a microcytic type, reticulocytosis, increased fragility of the red blood cells, spherocytosis with the volume normal or increased, acholuric jaundice, and an elevated icterus index and splenomegaly. There is no itching of the skin in this type of jaundice. The congenital type appears in infants and children. The acquired form usually appears after 20 years of age, is more severe, and has exacerbations or "crises" of malaise, abdominal pain, increased jaundice with the associated blood findings, more pronounced anemia, fever and rapid increase in the splenomegaly, accompanied by abdominal pain. The high incidence of associated biliary calculi, 60 per cent, adds a confusing and complicating feature to this otherwise clear diagnosis. Whereas the stools in ictero-anemia have normal amount of bile, a complicating stone obstruction in the common duct renders them acholic.

Doan found the conditions existing in thirteen families, twelve of whom had no knowledge of it, although one member in each generation had it. The importance of recognizing that constitutional defect lies in the fact that a fatal relapse or exacerbation may be precipitated by an infection or trauma at any time. Diamond reports on the study of twenty-five cases of this disease in children. In five, operation was refused with resultant death in two. Splenectomy was done in twenty, of whom eighteen have been completely relieved of all symptoms; one died of mesenteric thrombosis and one was relieved but not cured. He feels that this disease in children may not progress in as benign a fashion as it often does in adult life; also, that the younger the patient at the onset, the more severe the condition tends to become. The infant with the disease may not be able to wait for a second crisis before a splenectomy is performed. In children, delay also spells growth disturbances in the skeleton and other organs, even mental retardation as well as gallstone formation. Early splenectomy is indicated. Pemberton (1940) reports 165 patients with hemolytic icterus treated by splenectomy with a hospital mortality of 3 per cent and a most enviable survival record, namely, 88 per cent five-year and an 80 per cent ten-year survival rate (Table VIII).

The treatment for this condition is splenectomy which produces phenomenal results; that is, permanent and positive cure. Care must be

TABLE VIII

HEMOLYTIC JAUNDICE MORTALITY

AUTHORS	MORTALITY (%)
Pemberton (1931)	3.4
Doan (1934)	0
Pemberton (1940)	3
Diamond (1938)	5
Andrus and Holman	0
Rousellot (1938)	6.6
Eliason and Stevens (1942)	0

taken, however, to have an indubitable diagnosis. Atypical cases are not helped by surgery on the spleen. It is much wiser to operate upon these patients in the remission period, although the surgeon's hand may be forced by the rapid uncontrolled acute phase. Doan mentioned seventy-five blood relatives with recognized trait in forty. Seventeen of these had a splenectomy done, five of whom had a blood count of only one million. There were no deaths despite the fact that medical care has accomplished nothing except to bring the patient to surgery in a precarious condition. It has frequently been shown that patients can live with this chronic state of anemia due to continued hemolysis for many years relatively normally so one should not rush into surgery. We saw a young woman of this sort who had reached the age of 35 years and had had four children and was pregnant again when seen by us.

Removal of the spleen was first done for this condition fifty-five years ago. This patient is known to have lived forty-five years.

Thompson (1938) also reports from the Spleen Clinic in New York thirty splenectomies for this disease with an operative mortality of two, or 6.6 per cent, with an excellent result in this condition in twenty-six of the others for follow-up periods ranging from one to eighteen and one-half years. Biliary calculi were found at operation in four of the patients in this group. Thirteen cases treated conservatively were all found unimproved in follow-up reports ranging from 7 to 39 years (Table IX).

TABLE IX

HEMOLYTIC JAUNDICE

FOLLOW-UP DATA

AUTHORS	5 YR. (%)	10 YR. (%)	45 YR.
Pemberton (1940)	89.3	80.4	
Diamond (1938)	90		
Literature			1
Rousellot (1938)	26	10	
Eliason and Stevens (1942)	50	15	

Ninety per cent returned for follow-up.

He concludes that splenectomy promptly, completely, and permanently relieves these patients but that this operation does not benefit the atypical hemolytic anemias.

Conclusion.—The above data indicate that splenectomy is the treatment of choice in true, congenital ictero-anemia. In the acquired or adult form, mild in character, splenectomy is not necessarily the treatment indicated.

TECHNIQUE

The operation of splenectomy may be a very difficult one or a relatively simple one, depending upon the size of the spleen and the presence or absence of adhesions. The left rectus incision is probably the most frequently used. The lower pole of the spleen is delivered first and brought

out of the wound. The upper pole of the spleen then may be exposed. By using this procedure, the size of the incision need not be so large as would otherwise be required. When the spleen is very large, it may occasionally become necessary to make a lateral transverse extension of the incision at the lower end. This gives considerable additional exposure. Such a step is seldom required but may be a valuable aid when an especially large spleen is encountered. Some surgeons find the left paramedian or the left subcostal incision preferable to the left rectus incision.

By means of the gloved finger, the spleen is freed posteriorly. In this manner the capsule is not torn. The lienorenal ligament may occasionally have to be nicked with an instrument. The lower pole of the spleen is separated first and brought out of the incision. As this is done, the upper part of the spleen can be exposed. When the posterior attachment has been completely freed, the spleen is turned up to expose the posterior aspect of the pedicle devoid of a peritoneal covering. The peritoneum is then slit over the anterior aspect of the pedicle and the splenic vessels are exposed. Care must be taken that the tail of the pancreas, the stomach, and the retroperitoneal duodenum are sufficiently pushed aside before hemostats are applied. The vessels are clamped close to the spleen which is then removed. The vessels are doubly ligated. Wise has suggested the use of a rubber-shod clamp across the entire pedicle until the vessels are ligated individually. It would seem that he has minimized the possibility of damage to the pancreas by this procedure. The oozing from the bed of the spleen is usually so insignificant that no drainage is necessary. When the ooze is sufficient, a Penrose drain may be inserted. The drain is best brought out through a stab wound lateral to the incision.

When a large spleen has been removed, an abdominal binder is applied immediately to help maintain abdominal pressure. Pitressin is given every fourth hour for the first forty-eight hours. The convalescence may be marked by a moderately febrile course which is frequently quite prolonged. This is probably due to a thrombophlebitis of the splenic vein as mentioned by Bryce. No deaths due to extension of the thrombosis into the portal vein have been recognized in our personal series.

SUMMARY

An extensive review of the literature of the last ten years has been made and a statistical report compiled showing the mortality and life expectancy following splenectomy in cases of splenic anemia, thrombocytopenic purpura and ictero-anemia. Added to these is a similar report on sixty-three personal cases.

The technique of splenectomy is discussed.

CONCLUSIONS

Splenectomy gives the patient with splenic anemia the best chance. The earlier in the disease that splenectomy is done, the lower the surgical

mortality and the greater the life expectancy. It is the opinion of one of us (E. L. E.) that this is the only choice with cirrhosis. The operative mortality should not be over 10 per cent at the worst, and some of the patients have lived twenty years.

Cases of chronic hemorrhagic purpura that do not respond to conservative therapy should be subjected to splenectomy. In acute or fulminating purpura hemorrhagica, if the bleeding does not respond promptly to conservative measures, splenectomy should be performed early before the patient's condition is critical. A careful elimination of infection is important in the prevention of recurrent purpura. Recurrence of a serious nature is unusual.

Splenectomy is the treatment of choice in hemolytic jaundice, particularly in children. It is preferable to perform the operation during a remission, but occasionally it is necessary to remove the spleen during an acute exacerbation. The results following splenectomy are good in a high percentage of cases. In adults splenectomy is not always necessarily indicated.

SHOCK: THE PHYSIOLOGIC AND CLINICAL ASPECTS

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THE modern therapy of shock is based on a thorough understanding of the physiologic changes occurring in the injured patient. Peripheral circulatory failure of the hematogenic (Blalock) type is always associated with a diminution of the effective circulating blood volume whether this be due to hemorrhage, trauma, or burns. The exact mechanism producing this depletion may be in dispute, but experimental and clinical investigation has developed methods of estimating the relative amounts of fluid, protein, and red blood cells which will be lost in certain types of injury. There are definite changes which occur in the blood of the patient in shock, and some of these contribute to the development of the shock state while others probably perpetuate it. All of these factors cannot be corrected, but it is possible to attempt replacement of the fluid and protein which is lost and thus improve the circulation and overcome tissue anoxia. A fundamental premise of therapy is the realization that hematogenic shock does not develop instantaneously, and that the clinical appearance of hypotension is the gross evidence of time-consuming changes in the circulation.

In order to provide a background for rational therapy it is necessary to evaluate certain fundamental changes which occur in the circulation during the development of shock. It is not sufficient to define shock because of the variations in the theories of its mechanism; each author's definition will vary according to his personal concept, and will stress the factors which he believes most important. Blalock has considered it as "peripheral circulatory failure resulting from a discrepancy in the size of the vascular bed and the volume of intravascular fluid." This does not condemn any one theory, and provides as thorough an understanding as our present knowledge will permit. There are four outstanding theories as to the mechanism of the fluid loss in shock: (1) local loss of blood and fluid, (2) toxemia causing generalized capillary permeability, (3) vasoconstriction, (4) nociceptive impulses. These theories have been discussed in detail in recent reviews of the subject, and no attempt will be made to analyse critically the evidence for or against them.

In spite of the disagreement over the mechanism of shock there are many physiologic changes in the circulation which are of basic importance. The decreased effective circulating blood volume has been mentioned. Freeman and others[1, 2, 3] have shown that there is peripheral vasoconstriction resulting in a diminished peripheral blood flow. There

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is a fall in the venous as well as the arterial blood pressure,[4] and the cardiac output is decreased.[5, 6] The oxygen saturation of the blood is decreased,[2] and there is diminished oxygen consumption by the tissues. A large amount of plasma protein disappears from the circulation,[7] and because of the preponderant loss of plasma the red cell hematocrit becomes concentrated. There are other factors which may occur, but which may not be of primary significance: plasma potassium increases,[8] tissue anoxia develops, and there may develop a generalized capillary permeability. The role of the adrenal cortex and of tissue metabolites or toxins has not as yet been definitely established.

A great deal of confusion has arisen because of attempts to classify shock as primary and secondary. Primary shock is defined as the state of circulatory collapse which occurs almost immediately after an injury and is characterized by subnormal temperature, cool perspiring extremities, pallor, rapid pulse, and low blood pressure. This condition may occur within one-half an hour following a head injury, a perforated ulcer, or in association with spinal anesthesia or with drugs such as histamine. The patient often shows rapid improvement following relief of pain, or sometimes even without treatment. In this instance the fall in blood pressure is probably due to a rapid increase in the size of the vascular bed following capillary dilation while the blood volume remains essentially unchanged. As soon as the tonus of the peripheral circulation improves, normal circulatory balance is established, and the blood pressure rises. This condition differs markedly from that existing in the patient who gradually develops circulatory collapse several hours after injury and who is said to be suffering from secondary shock. This patient has had an actual loss of effective blood volume from the circulatory bed and the blood pressure falls in spite of compensatory peripheral vasoconstriction. Blalock[6] has suggested an admirable classification of shock which is of value in differentiating these types. He suggests that the term primary shock be replaced by (1) neurogenic, the fall in blood pressure resulting from pain, spinal anesthesia, etc., and (2) vasogenic, that resulting from histamine, anaphylaxis, etc. The term hematogenic is reserved for shock resulting from an actual decrease in effective blood volume.

The classification of these types of shock will not be confusing if the entire clinical picture is correlated with the type and extent of the injury and the period of time which has elapsed since the injury occurred. Unless the patient has had a rapidly exsanguinating hemorrhage, an early fall in blood pressure, with other signs of shock, may not mean serious derangement of the circulation, and the response to treatment may be very rapid. If, however, the circulation is not improved, early neurogenic shock may result in a true hematogenic type, i.e., because of the sluggish circulation, tissue anoxia may develop with resultant damage to the capillaries and an increase in their permeability. The classical signs of shock are the late manifestation of a process which

begins immediately after an injury. It is of the utmost importance to realize that the blood volume may decrease by as much as 50 per cent, and the blood pressure remain normal because of vasoconstriction. The replacement of fluid loss is of most value before the circulatory depletion has become extreme and before the shock state has become irreversible. It therefore would seem more logical to evaluate the process as a whole rather than to wait for obvious circulatory changes before instituting therapy. The prevention of profound circulatory collapse is possible in many instances in which it would be fatal to await the obvious changes. The value of the hematocrit, blood, or plasma specific gravity, and plasma protein concentration in predicting and evaluating shock will be discussed.

RECOGNITION OF SHOCK

1. *General Condition of the Patient.*—An accurate evaluation of the general appearance of the patient together with type and extent of the trauma form the most practical clinical method of recognizing impending shock. The degree of shock is, in general, in direct proportion to the amount of tissue damage and the time which elapses before treatment is instituted. The patient who appears apathetic, who is pale, and whose extremities are cold and clammy within a few hours after injury may already have a marked reduction in blood volume in spite of a nearly normal blood pressure.

2. *Pulse.*—The onset of shock is usually associated with a rapid thready pulse, but, both in the experimental animal and in man, a bradycardia may occur in profound shock.[7]

3. *Blood Pressure.*—The arterial blood pressure has long been considered the classical criterion of shock. In the experimental animal, the blood pressure may be normal at a time when the circulating plasma volume is half the normal, only to fall precipitously just before death.[7, 9] That the arterial blood pressure is an unreliable guide has long been recognized, because the vascular bed is gradually decreased by vasoconstriction until the vasomotor center fails and collapse occurs. Although the venous pressure decreases as shock develops, it must be considered an unreliable clinical guide. The hydrostatic pressure of the vein, the muscle pressure,[10] and the slowed peripheral blood flow make venous pressure determinations unreliable unless performed under carefully controlled conditions. The pulse pressure is often of value in detecting early shock; as peripheral vasoconstriction occurs the diastolic pressure may increase with a consequent decrease in pulse pressure. A patient with a gunshot wound of the abdomen was found to have a 50 per cent decrease in circulating plasma volume; his blood pressure was 120/100. After recovery his normal blood pressure was found to be 120/70. This change is not always evident, but when present is significant.

4. *Hematocrit.*—The hemoconcentration associated with shock has been emphasized by Moon[11] and others. In shock produced by intestinal

manipulation the hematocrit rises as the plasma volume decreases.[7] The hematocrit is of minor significance in shock due to hemorrhage since the remaining blood is diluted by tissue fluids and the hematocrit decreases. If the shock is due to trauma or operative procedures, the hemoconcentration, unfortunately, varies in degree, and individual determinations may be of little value. A hematocrit of 45 per cent may indicate hemoconcentration in a patient who has an anemia, but this would not be evident unless a control determination were available. If the hematocrit is markedly increased the individual determination is of value, but if not, the trend of at least two determinations must be known. It thus becomes of limited value in the evaluation of a patient in the accident ward. The hemoconcentration of the burned patient is of unquestionable value, and this will be discussed later.

5. *Plasma Specific Gravity and Plasma Protein Concentration.*—Scudder[8] has emphasized the increase in plasma and blood specific gravity which occurs in shock, and he feels that this can be used in the clinical evaluation of the shocked patient. The specific gravity of plasma will not increase unless more fluid than protein is lost from the circulation, and dehydration is not the outstanding feature of shock during the early stages. Large amounts of protein are lost from the circulation whether the shock is due to trauma or burns, and this loss may occur so rapidly that the plasma specific gravity decreases rather than increases. In experimental shock produced by intestinal trauma the specific gravity decreases (Fig. 1). This decrease has been uniform in

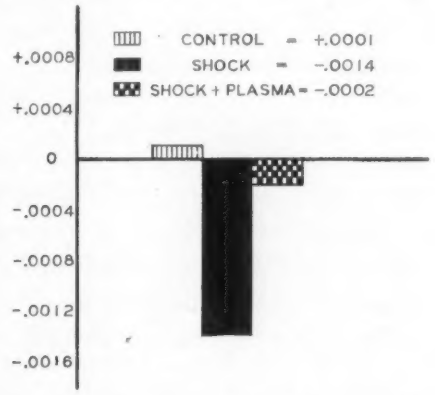

Fig. 1.—Graph showing specific gravity in experimental shock.

all of the experiments in which the animals developed peripheral circulatory failure, and in general the most marked fall of the specific gravity occurs in the animals most profoundly shocked. When these animals are treated with plasma, the rise in blood pressure is usually associated with an increase in the plasma specific gravity.

Specific gravity determinations have been done at frequent intervals during abdominal operations which resulted in varying degrees of peripheral circulatory failure. The specific gravity has shown a definite

tendency to decrease with the development of shock when no fluid therapy was given. The patients who were in shock and received adequate plasma replacement therapy responded with an increase in or maintenance of the specific gravity. In early burn shock the plasma specific gravity may also decrease. In our experience it has been difficult to prevent the specific gravity from falling by administering adequate plasma, and the problem of increasing plasma protein concentration has not occurred. If a burn has been neglected, secondary dehydration may develop, but this is not a factor in the initial treatment. The initial loss of protein in and around the burned area is so great that the plasma specific gravity decreases. This should not be confused with the concentration of the hematocrit, but should be considered as a separate change.

TREATMENT OF SHOCK

The importance of the early recognition of impending shock has been stressed because it is in the early stages that replacement therapy can be most effectively accomplished. The decreased blood pressure of hematogenic shock develops only after there has been a marked decrease in blood volume and the circulation is no longer able to compensate by peripheral vasoconstriction. If the blood volume can be replenished before this advanced stage is reached, many of the deleterious effects of peripheral circulatory failure may be avoided, and the patient will respond more favorably. The injured patient should be treated as soon as possible; an hour's delay may mean the difference between irreparable circulatory damage and compensable impending failure. The compound fracture should not be débrided or the burn treated locally until blood or plasma is available and intravenous injection started. One of the greatest errors of clinical judgment is to underestimate the seriousness of an injury, and to have the patient develop the classical signs of shock on the operating table without having received adequate shock therapy. The ease with which blood or plasma may be preserved no longer permits the excuse that proper fluid was not obtainable.

The treatment of shock may be divided into two main categories: (1) General features including oxygen and drug therapy, and (2) fluid replacement.

General Features.—The injured patient should be made as comfortable as possible and small doses of morphine are not contraindicated after the extent of the injury has been determined. Major bleeding should be controlled and compound fractures should be temporarily immobilized to prevent further damage to the soft tissues. The patient should be kept warm, but Blalock and Mason[12] have shown that overheating may be deleterious. At the present it seems most advisable to conserve body heat by means of blankets, etc., but excessive external heat is contraindicated. The foot of the bed or stretcher should be elevated to promote venous return from diminished peripheral circula-

tion. The administration of a high concentration of oxygen is of value in combating the anoxemia of shock. Wood, Mason, and Blalock[13] have demonstrated experimentally that an increase in oxygen content of arterial and venous blood is beneficial in the shocked animal, and clinical experience has confirmed their observations.

The use of vasopressor drugs such as adrenalin and ephedrine should be discouraged. Freeman and others[2] have shown that shock may be produced by prolonged administration of adrenalin. Compensatory peripheral vasoconstriction is already present in hematogenic shock, and further constriction may lead to increased capillary stasis and anoxemia. Small amounts of ephedrine or adrenalin are permissible in the early neurogenic shock, but the patients should be carefully selected.

Adrenal cortical extract is being recommended in shock on the theory that it will prevent or decrease capillary permeability. The work of Swingle and others[14, 15] has resulted in favorable reports of its efficacy. Rhoads[16] has used adrenal cortical extract in conjunction with plasma in treating burned patients. Their results indicate that less plasma is required to maintain the blood volume if adequate adrenal cortical extract is used. Although these results seem definite, the response of the burned patient is variable, and great care must be taken in evaluating clinical results. This is by no means a condemnation of the extract, but merely a reservation of final opinion until this method of treatment has withstood the test of extensive clinical evaluation. In our clinic, burns of apparently equal severity have been treated with and without the extract with no appreciable difference in protein and fluid requirements. If there is a generalized increase in capillary permeability in secondary shock, the method is sound; if all the fluid is lost at the site of the damaged capillaries it would seem of less value.

Fluid Replacement.—The most fundamental aspect of the present-day treatment of shock is the replacement of the various elements lost from the circulation. The proper treatment demands an understanding of the relative proportion of red cells, fluid, and protein which are lost in various types of hematogenic shock. Fig. 2 is a schematic representation of the relative amounts of the three elements present in the blood stream when the decreased blood pressure is due to (1) dehydration, (2) hemorrhage, (3) trauma, and (4) burns. The electrolytes and other components of the plasma are disregarded for purposes of simplicity. The dehydrated patient requires only the parenteral injection of normal saline solution. The total circulating protein and red cells have not been depleted.

When the blood volume is depleted by hemorrhage the protein, fluid, and red cells are lost in the same proportion as they existed in the blood. If the hemorrhage has been minor, the volume may be restored with saline solution or, if more extensive, whole blood should be used.

The body will tolerate extensive loss of red cells, but a serious hemorrhage may result in a serious loss of protein. If the circulation is restored with plasma, red cells may be mobilized from areas of stagnation or reserve sources. Brennan[17] has shown that an actual increase in circulating red cells may result from plasma injections following hemorrhage. Slow prolonged hemorrhage may result in the visceral changes of traumatic shock, and require the same type of treatment.

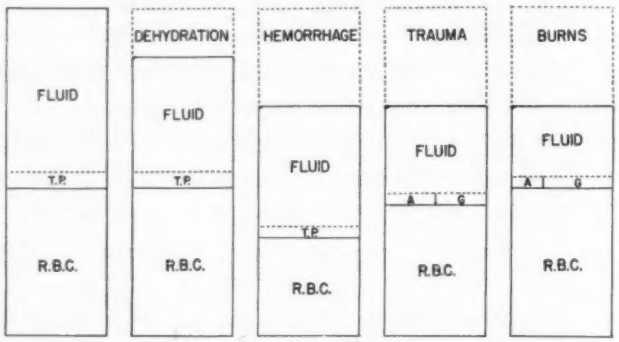

Fig. 2.—Schematic representation of shift of blood components in shock.

In traumatic shock whole blood is lost at the site of injury, but there is an excessive loss of plasma from the damaged capillaries. Consequently, the total volume of red cells may be decreased, but the most marked decrease occurs in the fluid and protein elements of the circulation. Actual determinations of the plasma volume may indicate a 50 per cent reduction of fluid. Although the concentration of circulating plasma protein may be normal or only slightly decreased, the total circulating protein is greatly reduced. The intravenous injection of saline solution is detrimental. The saline solution causes dilution of the remaining protein and a resultant decrease in colloid osmotic pressure. It may cause a temporary increase in blood pressure, but the increased hydrostatic pressure will result in further protein loss and more profound shock. Plasma or whole blood should be used in traumatic shock to replace adequately the depleted circulation. The large amounts necessary must be emphasized, as 1,500 or 2,000 c.c. of blood or plasma are often required to replenish the blood volume of the adult in shock.[9]

The shock resulting from burns is almost entirely due to plasma loss in the vesicles of the burn and in the underlying tissues. The volume of red cells remains essentially unchanged and the hematocrit increases. The plasma volume is greatly reduced and a tremendous amount of plasma protein is lost. The fluid in the vesicles contains 4 to 5 Gm. per cent of protein. Since about 90 per cent of this protein is albumin, an inversion of the albumin-globulin ratio results. It is of interest to note that in recently burned patients the loss of protein is so great that the plasma specific gravity and protein concentration decreases.

For this reason, the burned patient requires very large amounts of plasma to replenish the fluid and protein. Saline injections are as deleterious in burns as in traumatic shock because of protein dilution and resultant edema.

A comparison of the response of two burned patients to fluid therapy emphasizes the importance of carefully analyzing the changes as they occur in the circulation. Patient G. S. (Fig. 3) was admitted to the hospital in profound shock with second- and third-degree burns of the

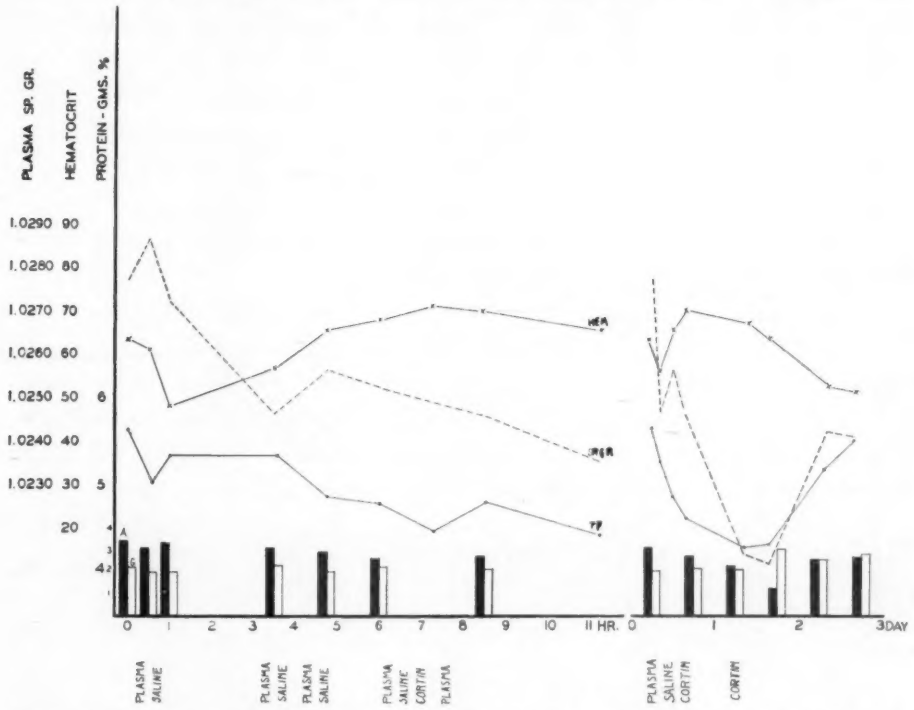

Fig. 3.—Graph of hematocrit and plasma levels after extensive burns in Patient G. S.

entire trunk, face, neck and both arms. The severity of the shock is indicated by the fact that his blood pressure did not reach a normal level for thirty-six hours in spite of intensive fluid therapy. This patient received a total of 2,200 c.c. of plasma and 6,600 c.c. of saline solution during the first twenty-four hours with a resultant marked decrease in the plasma specific gravity. His condition was so serious that it was impossible to adequately débride and treat the burned area; however, tannic acid and silver nitrate were applied to decrease local fluid loss. Actually he required an amount of fluid greater than his entire blood volume to maintain the circulation in spite of the use of adrenal cortical extract. It is obvious from the decrease in the plasma specific gravity and protein concentration that he should have received much more protein and less saline solution. The albumin-globulin ratio became inverted by the second day, and this is due to the greater loss of albumin than globulin in the burned area. This case also illustrates

the possibility of error inherent in the specific gravity determination of protein concentration. Plasma protein analyses were performed by the micro-Kjeldahl method as a check on the specific gravity. There is a close relationship between the results obtained by the two methods when the albumin-globulin ratio is normal, but the specific gravity interpretation is less accurate when the albumin-globulin ratio is reversed. The hematocrit remained concentrated during the first twenty-four hours, but on the second day returned to the normal level.

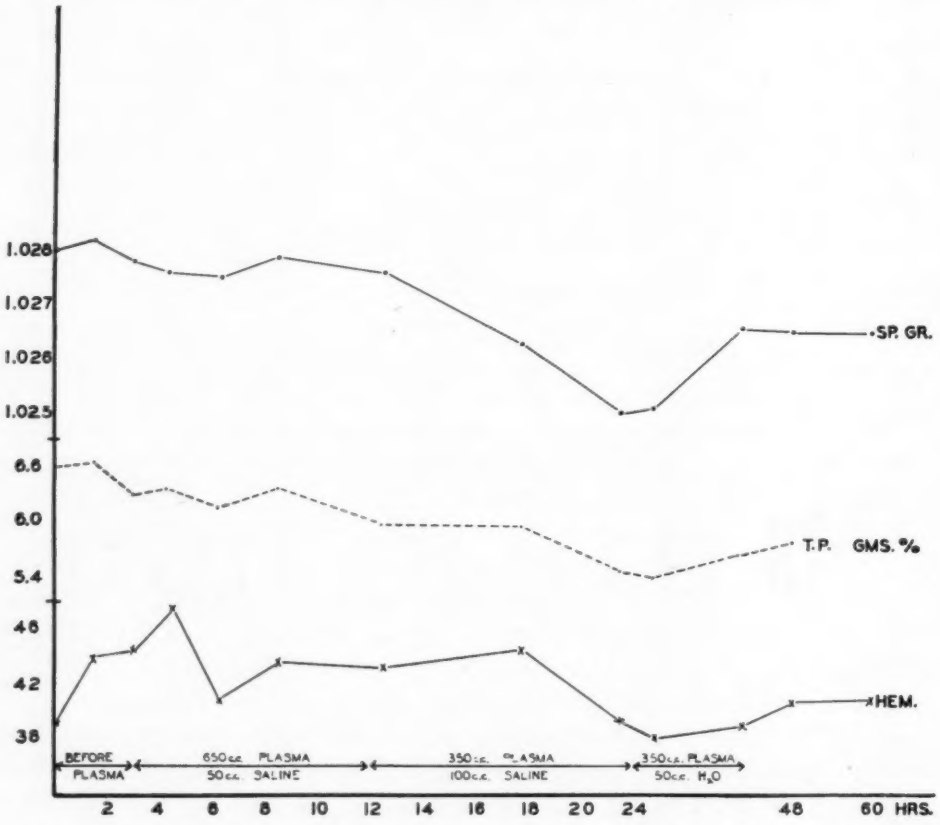

Fig. 4.—Graph of hematocrit and plasma levels after extensive burns in a 9-year-old child.

The second case illustrated is that of a 9-year-old girl who had received second- and third-degree burns of the trunk and arm involving about 30 per cent of the body surface (Fig. 4). The plasma specific gravity and protein concentration were maintained at a normal level by the injection of whole plasma and comparatively little saline. Her course during this period was uneventful, the blood pressure was maintained, temperature did not rise above 38.5° C., she tolerated fluids by mouth, and the urinary output was adequate. Although she was not as extensively burned as the first patient, the various observers agreed that she would have developed peripheral circulatory failure

without adequate therapy. The local burn was treated with sulfadiazine in triethanolamine.

Each burned patient must be evaluated as an individual problem. The red blood count and hemoglobin should be determined at frequent intervals. If facilities are available the red cell hematocrit, plasma specific gravity, and protein concentration yield valuable information in determining fluid therapy. In our experience the specific gravity and protein concentration have been found to decrease rather than increase during the first few hours before plasma is started. It is true that the specific gravity might have increased if treatment had been deferred sufficiently long to allow dehydration to develop. This early fall in specific gravity can be readily explained by the tremendous loss of fluid and proteins into the vesicles and into tissues beneath the burned area. The greatest loss of protein occurs during the first twenty-fours hours, and whole plasma is usually necessary to compensate for this loss. There is relatively less protein lost during the second twenty-four hours, but in severe burns parenteral protein injections are still necessary. The hematocrit may fall below normal by the third or fourth day, necessitating whole blood transfusions. The necessity of determining the blood nonprotein nitrogen and chlorides should be stressed. No hard and fast rule of fluid therapy will be satisfactory in all patients, and only by careful attention to details can the patient be adequately treated.

CONCLUSIONS

1. The early recognition of shock and its therapy depend on a knowledge of the physiologic changes occurring in the failing circulation.

2. There is no single diagnostic criterion by which impending circulatory failure may be recognized and at the present time the diagnosis depends on a general evaluation of the patient. The inadequacy of single hematocrit and plasma specific gravity determinations has been stressed.

3. The plasma specific gravity may decrease rather than increase in the early stages of shock.

4. Adequate fluid therapy depends on the relative amounts of red cells, fluid, and protein which must be restored to the circulation.

5. Fluid therapy is most efficient when instituted before the patient develops the classical signs of shock.

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STUDIES OF THE ARTERIAL OXYGEN SATURATION IN THE POSTOPERATIVE PERIOD AFTER PULMONARY RESECTION

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ANOXIA, or oxygen want in the tissues, has widespread detrimental effects that have been recognized for some time and many investigations on this subject have been published recently. Since one of the chief causes of anoxia is impairment in the oxygenation of the blood as it passes through the lung, one might expect to encounter anoxia following major thoracic operations. Clinically, however, oxygen want is often undetected, and the significance of anoxia of slight degree is not sufficiently appreciated. Little is known of the severity, frequency, and duration of oxygen want after pulmonary resection. In the present investigation several hundred determinations of the arterial oxygen saturation have been made in the postoperative period in order to obtain an accurate estimate of the degree of anoxia after the various types of major thoracic procedures, and these values have been compared in most instances with preoperative determinations. Special attention has been given to cases of pulmonary resection.

It should be emphasized that no attempt is made to evaluate all aspects of anoxia in thoracic surgery on the basis of the data here reported. We have studied the occurrence of lowering of the oxygen saturation of the arterial blood, that is anoxic anoxia, and we have some information about anemic anoxia from oxyhemoglobin capacity determinations, but to date we do not have accurate information concerning the importance of stagnant anoxia in thoracic surgery.

The recognition of lowering of the oxygen saturation of the arterial blood is of considerable clinical importance. The anoxia encountered after thoracic surgery usually can be corrected by the administration of an adequate concentration of oxygen by inhalation therapy. If untreated, the anoxia may be the forerunner of numerous postoperative complications.

TECHNIQUE

A determination of the arterial oxygen saturation was usually done within the first few days after operation, and often on the first postoperative day. Additional determinations were made during the postoperative period, but none was made during the first few hours after operation when the effects of a general anesthesia were still present.

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In most instances the patients were receiving sedatives and narcotics during the period in which the studies of the arterial oxygen saturation were made, but rarely was the blood sample taken shortly after a narcotic was administered. Moreover, the doses of morphine employed were small. If the patient was receiving oxygen therapy, as was frequently the case in the early postoperative period, he was removed from the oxygen tent, or the oxygen by catheter or mask was discontinued for a period of at least thirty minutes, and usually over an hour, before the arterial blood was taken. It is recognized that even an hour after discontinuing oxygen therapy the blood may not have returned to its basic level of unsaturation, especially if the degree of anoxemia is severe. In some instances the taking of the blood was postponed for a day or so because it was considered inadvisable to discontinue the oxygen therapy even for one-half hour.

The arterial blood for analysis was obtained from the brachial artery under anaerobic conditions. The blood was drawn into pipettes within fifteen minutes of the time it was withdrawn from the artery. The oxygen content and oxygen capacity of the blood were immediately determined by the method of Van Slyke and Neill, and the per cent saturation calculated. All determinations were done in duplicate. In the method employed the normal range of saturation of the arterial blood with oxygen is 94 to 96 per cent except in older subjects in whom values down to 92 per cent may be regarded as normal.[1] We consider an arterial oxygen saturation of less than 90 per cent as indicating a clinically significant degree of anoxia. Less than 85 per cent saturation of the arterial blood indicates a relatively severe degree of anoxia.

The carbon dioxide content of the arterial blood was also determined, but since the results do not appear to be particularly significant the data on carbon dioxide are not presented.

MATERIAL

The oxygen saturation of the arterial blood was studied after a variety of thoracic surgical procedures, but particular attention was given to cases in which the patients had been subjected to pulmonary resection. A total of 17 patients was studied following pneumonectomy, and 13 of this group were followed until the arterial oxygen saturation returned to a normal level. The 4 remaining patients died in the postoperative period. Of the 17 pneumonectomy cases, 12 were total pneumonectomies, i.e., the lung was removed completely by hilar dissection, whereas in the remaining 5 cases a tourniquet was employed and a fragment of pulmonary tissue was left behind. In addition to these cases, there was one patient (M. K.) in whom all of the right lung except a small portion of the upper lobe was removed. This case will be discussed separately later.

A group of 21 patients was studied following lobectomy. In some of these cases a bilobectomy was done. In most instances the case was

followed in the postoperative period until a normal arterial oxygen saturation was found.

PNEUMONECTOMY

The results of the arterial oxygen saturation determinations after pneumonectomy are presented in Table I. In a few patients with a very satisfactory clinical course the arterial blood had a normal oxygen saturation within two to three days after removal of one lung. The majority of the patients, however, had slight reduction in arterial oxygen saturation for the first week after pneumonectomy. In no instance did the percentage saturation drop below 85 per cent at any time unless serious postoperative complications occurred.

In two cases there was a prolonged arterial oxygen unsaturation associated with a deviation in the position of the mediastinum. In one of these patients (E. B.) the clinical course was quite satisfactory but a large fluid accumulation on the operated side displaced the mediastinum into the normal side. Restitution of the mediastinum to a median position by the withdrawal of fluid resulted in a rapid return of the arterial oxygen saturation to a normal level. The other patient (D. M.) was a 62-year-old male with senile type of emphysema in both lungs and carcinoma of the left lung. Prior to the preoperative pneumothorax the arterial oxygen saturation was 90.7 per cent, which is almost normal for a man of his age. The arterial oxygen studies in the postoperative period were of great interest. The pneumonectomy was well tolerated as far as the surgical procedure was concerned. The arterial oxygen saturation dropped only slightly in the first few days after pneumonectomy. Although no surgical complications developed, the arterial oxygen saturation continued to drop gradually during the next three weeks. The pulmonary function was investigated and it was discovered that the residual air volume had reached the very high value of 70 per cent of the total lung volume. This finding indicated that because of the displacement of the mediastinum to the operated side the remaining lung was in a markedly overdistended state and as a result was not properly ventilated. In order to lessen the overdistention in the remaining lung a pneumothorax was induced on the operated side so that the mediastinum would be less deviated. With return of the mediastinum to approximately the preoperative position there was a rapid improvement in the arterial oxygen saturation associated with a decrease in the distention of the lung. The reason for the disturbance caused by the mediastinal displacement following pneumonectomy in this case was the pre-existing emphysema in the remaining lung. Following overdistention this already emphysematous lung could not adjust itself functionally as a normal remaining lung usually does after pneumonectomy.

LOBECTOMY

The results of the arterial oxygen determinations after lobectomy are presented in Table II. Following lobectomy the arterial oxygen satura-

TABLE I

PNEUMONECTOMY CASES

CASE	DATE	DURATION AFTER OPERATION	ARTERIAL OXYHEMOGLOBIN			REMARKS
			CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)	
R. B., aged 60; carcinoma of left lower lobe with atelectasis. Pneumonectomy, 10/21/39	10/17/39	Preoperative	14.3	14.9	96.9	Had bronchopneumonia 6 days postoperatively; gradual recovery. Auricular fibrillation present preoperatively and postoperatively
	10/24/39	3 days	14.6	15.5	95.1	
	10/27/39	6 days	12.9*	13.3*	98.1*	
	10/30/39	9 days	11.2	12.7	89.4	
	11/29/39	39 days	12.8	13.8	94.1	
	3/ 7/40	4½ months	18.7	19.4	97.1	
E. B., aged 31; carcinoma of left main bronchus with atelectasis of left lung. Pneumonectomy, 1/27/40	1/18/40	Preoperative	18.4	18.9	98.2	Pleural fluid on operated side displaced mediastinum to right during period of lowest arterial oxygen saturation; oxygen saturation became normal shortly after mediastinal deviation to unoperated side was corrected
	1/29/40	3 days	14.4	16.7	87.1	
	2/ 3/40	7 days	12.7	14.8	86.4	
	2/ 5/40	9 days	13.8	15.6	89.4	
	2/10/40	14 days	14.5	15.5	95.1	
	2/27/40	31 days	15.6	16.1	96.9	
T. G., aged 43; carcinoma of right main bronchus. Pneumonectomy, 9/28/39	9/21/39	Preoperative	18.4	19.5	95.0	Uneventful postoperative course
	9/29/39	1 day	17.0*	17.4*	98.6*	
	9/30/39	3 days	13.5	15.4	88.7	
	10/ 2/39	5 days	13.4	14.7	92.3	
	10/ 6/39	9 days	13.5	14.5	94.7	
	10/21/39	24 days	12.9	14.0	93.4	
J. H., aged 28; suppurative pneumonitis with multiple abscesses of right lung. Pneumonectomy, 5/23/40	2/29/40	Preoperative	13.6	15.0	91.4	Immediate postoperative condition satisfactory. Empyema drained on fifth postoperative day. Bronchus opened on eleventh postoperative day. Patient died on twelfth day
	5/ 1/40	Preoperative	15.2	16.2	94.4	
	5/25/40	2 days	10.2	10.7	97.3	
	5/29/40	6 days	12.3	12.9	96.8	
F. I., aged 46; old tuberculous stenosis of right main bronchus with bronchiectasis. Pneumonectomy, 5/19/41	1/23/41	Preoperative	19.7	20.5	97.0	Uneventful postoperative course
	5/21/41	2 days	15.6	17.6	89.5	
	6/ 3/41	15 days	13.6	14.6	93.6	

S. J., aged 30; giant cyst and bronchiectasis of left lung. Subtotal pneumonectomy, 7/17/40	7/29/40	12 days	10.8	11.6	95.0	Uneventful postoperative course
W. J., aged 53; carcinoma of right middle lobe. Pneumonectomy, 5/8/40	4/25/40	Preoperative	18.0	18.6	97.7	Uneventful postoperative course
	5/ 9/40	1 day	15.9	17.6	91.6	
	5/14/40	6 days	14.7	15.9	93.5	
	5/28/40	20 days	14.0	15.0	94.6	
	7/ 3/40	8 weeks	15.2	16.0	95.9	
	10/ 4/40	5 months	17.2	17.9	97.2	
N. N., aged 36; tuberculosis of left lung with residual cavity after thoracoplasty. Subtotal pneumonectomy, 11/15/39	10/30/39	Preoperative	18.4	19.5	95.3	Marked dyspnea and paradoxical motion postoperatively in spite of normal arterial oxygen saturation in oxygen tent. Died on second postoperative day
		2 days	15.4*	16.4*	95.0*	
E. R., aged 32; bronchiectasis of left lung. Pneumonectomy, 7/19/41	5/26/41	Preoperative	19.1	20.5	93.8	Uneventful postoperative course except for profuse bronchial secretions on second postoperative day
	7/21/41	2 days	15.0*	15.9*	95.5*	
	7/22/41	3 days	13.2	14.0	95.2	
	12/15/41	5 months	14.5	15.7	93.4	
J. L., aged 12; bronchiectasis of left lung. Subtotal pneumonectomy, 11/8/39	10/12/39	Preoperative	16.4	17.5	94.7	Postoperative course satisfactory except for empyema and bronchial fistula
	11/ 9/39	1 day	13.8	15.4	90.4	
	11/13/39	5 days	11.1	13.2	85.6	
	11/20/39	12 days	13.3	14.6	92.6	
	12/14/39	36 days	14.0	14.5	98.2	
	12/13/40	1 year	16.4	17.2	95.3	
A. M., aged 23; bronchiectasis of right lung with bronchostenosis. Subtotal pneumonectomy, 5/6/41	5/ 6/41	Preoperative	17.1	17.9	96.4	General condition good postoperatively. Postoperative empyema and amoebic dysentery
	5/ 7/41	1 day	15.2	15.8	97.7	
	5/13/41	7 days	14.0	15.2	93.4	
	7/ 8/41	63 days	14.3	14.9	97.2	
D. M., aged 62; carcinoma of left lung, bilateral fibrosis and emphysema. Pneumonectomy, 11/23/40	11/16/40	Preoperative	14.5	16.2	90.7	Postoperative condition quite satisfactory but arterial oxygen saturation continued to fall as mediastinal displacement toward operated side increased. Elevation of arterial oxygen saturation one month postoperatively coincident with restitution of mediastinum to midposition by introduction of air on side of pneumonectomy
	11/25/40	2 days	15.4	17.5	88.6	
	11/30/40	7 days	14.1	16.0	89.1	
	12/ 4/40	11 days	13.6	16.0	86.1	
	12/10/40	17 days	13.5	16.2	84.1	
	12/17/40	24 days	13.1	15.4	85.9	
	12/26/40	33 days	15.2	16.8	91.4	
	1/20/41	58 days	15.8	17.8	90.4	
	7/28/41	8 months	14.2	15.8	90.6	

TABLE I—CONT'D

CASE	DATE	DURATION AFTER OPERATION	ARTERIAL OXYHEMOGLOBIN			REMARKS
			CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)	
W. R., aged 45; carcinoma of right lower lobe. Pneumonectomy, 12/6/39	11/28/39	Preoperative	16.7	18.9	89.2	Postoperative pneumonia with profuse bronchial secretions. Died on second postoperative day. Last blood determination made shortly before death
	12/ 8/39	2 days	10.3*	17.8*	58.2*	
M. S., aged 26; pulmonary tuberculosis with residual cavity and bronchocutaneous fistula following thoracoplasty. Pneumonectomy, 6/24/40	9/22/39	Preoperative	15.3	16.7	92.7	Died postoperatively
	6/29/40	5 days	18.6*	19.2*	97.7*	
G. T., aged 21; bronchiectasis of left lung, previous thoracoplasty. Pneumonectomy, 7/15/41	3/ 8/41	Preoperative	16.0	17.6	91.6	Postoperative course satisfactory
	7/23/41	8 days	11.0	12.2	91.6	
	9/12/41	2 months	13.9	14.5	96.8	
V. W., aged 64; carcinoma of left upper lobe. Pneumonectomy, 8/3/40	8/ 2/40	Preoperative	15.8	17.2	93.1	Uneventful postoperative course
	8/ 5/40	2 days	14.5	15.5	94.7	
	8/10/40	7 days	12.7	13.8	92.8	
	10/10/40	9 weeks	14.8	15.8	95.1	
	2/24/41	5½ months	18.4	19.8	93.8	
W. H., aged 47; carcinoma of left main bronchus with atelectasis of left lung. Pneumonectomy, 1/15/40	1/17/40	2 days	17.5	18.4	94.8	Uneventful postoperative course
	1/23/40	8 days	18.6	20.3	92.9	
	4/ 5/41	15 months	18.7	19.8	95.6	
M. K., aged 36; suppurative pneumonitis of right lung. All of right lung removed except small portion of upper lobe, 8/12/39	8/19/39	7 days	10.6	12.5	86.0	Headache and anorexia for several weeks postoperative. Residual portion of right lung re-expanded slowly
	9/ 8/39	27 days	11.6	13.1	89.8	
	9/13/39	32 days	14.6	16.8	88.1	
	9/18/39	37 days	16.8*	17.2*	99.2*	
	10/ 2/39	7 weeks	15.8	17.0	94.3	

*Patient receiving oxygen at time of determination.

tion returned to a normal level somewhat more slowly than in the uncomplicated pneumonectomy cases. Most of the determinations made within a week of operation revealed some anoxic anoxia. In most of the cases in which the arterial oxygen saturation remained abnormally low for more than a week postoperatively some interference with pulmonary ventilation was present. In a few instances, however, the arterial oxygen saturation was low for a period of over a week in spite of excellent re-expansion of the remaining lobe on the operated side and in the absence of any postoperative complications. The explanation of this finding is apparently a temporary impairment in the correlation of ventilation and circulation in the remaining pulmonary tissue on the operated side. If, after lobectomy, difficulty is encountered in re-expansion of the remaining lobe on the operated side, several weeks may elapse before the arterial oxygen saturation reaches a normal level. In the case of G. M. the remaining lobe did not re-expand, but the arterial oxygen saturation nevertheless gradually became normal. If pleural fluid accumulates due to inadequate drainage after lobectomy, the remaining lobe may be compressed and oxygenation of the blood interfered with. If a pneumonic process develops in either lung, anoxia may result. The retention of bronchial secretion may lead to severe anoxia as well as atelectasis and pneumonic infiltration. Other factors are diminished respiratory movements and mediastinal displacement. Abnormalities of the remaining pulmonary tissue, especially emphysema and fibrosis, are of great importance.

A small amount of lung tissue which is poorly aerated, but still well perfused with blood, may significantly affect the arterial oxygen saturation. This is well illustrated by a case of bronchiectasis (M. K.) in which the right lower and middle lobes as well as a large part of the right upper lobe were removed. The remaining portion of the upper lobe re-expanded slowly. The arterial oxygen saturation remained between 86 and 90 per cent for six weeks after operation and did not reach a normal level until two months after operation. During most of the postoperative period there was no dyspnea or cyanosis but the patient complained of anorexia and headache which were improved by oxygen therapy. It seems probable that the remaining portion of the right upper lobe was perfused with blood from the pulmonary artery before adequate ventilation of these alveoli was restored. Had a total pneumonectomy been done instead, the arterial oxygen saturation would probably have reached a normal level much more rapidly. (Table I).

The effect of a bronchocutaneous fistula on the arterial oxygen saturation was studied in one case. When a large bronchial fistula develops after pneumonectomy, it is obvious that severe degrees of anoxia may result from interference with adequate ventilation of the remaining lung. We studied a case in which a moderate-sized fistula developed after lobectomy. The findings are shown in Table III.

TABLE II

LOBECTOMY CASES

CASE	DATE	DURATION AFTER OPERATION	ARTERIAL OXYHEMOGLOBIN			REMARKS
			CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)	
K. B., aged 25; bilateral bronchiectasis. Right middle and lower lobe lobectomy, 5/2/40; left lower lobe lobectomy, 7/9/41	5/ 2/40	Preoperative	17.1	18.6	92.5	Slow convalescence complicated by empyema and bronchopleural fistula after each operation
	5/ 8/40	6 days	12.3	13.9	89.3	
	6/16/41	6 weeks	15.3	16.3	95.0	
	7/11/41	2 days	13.2	16.4	81.7	
	7/14/41	5 days	13.9	16.0	87.8	
D. C., aged 26; bronchiectasis, left lower lobe. Lobectomy, 5/23/40	5/28/40	5 days	12.3	14.3	86.8	Postoperative empyema and bronchopleural fistula but general condition good
	6/ 4/40	12 days	11.9	14.1	85.3	
	6/10/40	18 days	13.3	14.2	95.3	
T. DeP., aged 31; bronchiectasis, right lower lobe. Lobectomy, 5/9/41	4/10/41	Preoperative	15.4	16.6	94.1	Satisfactory postoperative course
	5/12/41	3 days	11.8	13.6	88.7	
A. F., aged 25; bronchiectasis, left lower lobe. Lobectomy, 11/14/39	11/14/39	Preoperative	16.5	18.6	89.3	Postoperative course complicated by empyema and bronchopleural fistula; later developed tuberculous pneumonia in left upper lobe
	11/22/39	8 days	11.1	15.6	71.8	
	11/27/39	13 days	11.6	14.2	82.9	
	12/ 5/39	21 days	9.7	14.2	68.5	
	12/11/39	27 days	11.0	14.3	77.4	
	12/18/39	34 days	12.3	13.1	94.9	
	12/19/39	35 days	8.6	13.2	65.6	
	12/29/39	45 days	12.7	14.6	87.6	
	1/15/40	2 months	13.4	15.2	89.2	
	3/13/40	4 months	12.8	13.9	93.3	
F. H., aged 38; chronic suppurative pneumonitis. Right upper and middle lobe lobectomy, 4/24/41	4/25/41	1 day	14.1	15.7	91.1	Uneventful postoperative course

D. H., aged 26; bronchiectasis, right lower lobe lobectomy, 4/28/41	4/29/41	1 day	13.7	17.8	77.6	Clinically uneventful postoperative course
	5/ 5/41	7 days	11.9	13.7	88.0	
	5/13/41	15 days	12.2	13.3	93.0	
H. K., aged 25; bronchiectasis, right middle and lower lobe. Bilobectomy, 6/26/40	7/ 2/40	6 days	13.0	14.2	92.7	Retention of pleural fluid postoperatively; course otherwise satisfactory
	7/11/40	15 days	13.2	14.5	92.0	
	8/ 9/40	44 days	14.6	15.9	92.5	
J. K., aged 21; bronchiectasis, left lower lobe. Lobectomy, 5/13/40	4/26/40	Preoperative	13.8	15.4	90.6	Uneventful course postoperatively
	5/14/40	1 day	15.3	16.7	92.7	
M. L., aged 40; bronchiectasis left lower lobe. Lobectomy, 4/4/40	1/23/40	Preoperative	19.7	21.1	94.1	Postoperative empyema and bronchial fistula
	4/ 5/40	1 day	14.7	16.0	92.9	
	4/11/40	7 days	12.3	13.7	90.3	
E. M., aged 33; previous thoracoplasty for tuberculosis of left lung; bronchiectasis left lower lobe. Lobectomy, 6/2/41	7/11/41	39 days	14.7	15.6	95.4	Satisfactory postoperative course
R. McC., aged 48; bronchiectasis, right middle and lower lobes. Bilobectomy, 8/1/39	8/15/39	14 days	11.0	12.1	90.0	Satisfactory postoperative course except for empyema
	8/16/39	15 days	11.1	12.1	94.0	
	8/23/39	22 days	10.8	11.7	93.4	
E. M., aged 40; bronchiectasis, right middle lobe. Lobectomy, 11/13/40	11/14/40	1 day	13.7	15.2	91.3	Clinically uneventful postoperative course
	11/18/40	5 days	12.6	14.9	85.1	
	11/22/40	9 days	13.3	14.3	94.1	
G. M., aged 43; bronchiectasis, left upper lobe. Lobectomy, 9/27/39	10/ 4/39	7 days	11.6	13.3	88.8	Lower lobe, which was somewhat fibrotic, expanded poorly postoperatively
	10/ 9/39	12 days	10.5	12.8	83.4	
	10/12/39	15 days	11.1	12.4	90.9	
	10/24/39	27 days	11.9	12.8	94.4	
	11/ 9/39	6 weeks	14.6	15.4	94.7	
D. M., aged 26; bilateral bronchiectasis; situs inversus. Right lower lobe lobectomy, 7/23/41	7/ 7/41	Preoperative	17.9	18.4	98.2	Early postoperative course satisfactory; atelectasis of left upper lobe on seventh postoperative day
	7/24/41	1 day	16.0	16.6	97.6	
	11/27/41	4 months	13.8	15.1	92.5	

TABLE II—CONT'D

CASE	DATE	DURATION AFTER OPERATION	ARTERIAL OXYHEMOGLOBIN			REMARKS
			CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)	
C. M., aged 37; bronchiectasis; right middle lobe and lower lobes; emphysema. Bilobectomy, 7/13/40	6/24/40	Preoperative	17.5	19.4	90.8	Died postoperatively of bronchopneumonia and sepsis
	7/15/40	2 days	16.2*	17.2*	95.6*	
	8/ 1/40	19 days	12.8	14.2	91.4	
	8/ 3/40	21 days	13.8*	14.5*	96.5*	
C. P., aged 23; bronchiectasis, left lower lobe. Lobectomy, 6/5/41	6/ 6/41	1 day	16.9	20.3	83.9	Clinically uneventful postoperative course
	6/19/41	14 days	14.5	15.8	92.8	
M. R., aged 55; chronic pulmonary abscesses. Right upper and partial lower lobe lobectomy, 4/21/41	4/22/41	Preoperative	13.1	13.9	95.5	Poor expansion of remainder of right lung; postoperative empyema and pulmonary suppuration
	4/23/41	1 day	14.0	16.8	84.7	
	7/30/41	3 months	11.2	12.1	92.5	
J. R., aged 17; bronchiectasis, right upper lobe. Lobectomy, 5/29/41	5/21/41	Preoperative	18.8	20.2	96.4	Postoperative course quite satisfactory in spite of localized empyema and bronchial fistula
	6/ 2/41	4 days	11.5	12.8	91.5	
	6/19/41	21 days	15.3	16.1	96.1	
J. S., aged 38; bronchiectasis, right lower lobe. Lobectomy, 11/2/39	11/ 2/39	Preoperative	13.4	14.5	93.6	Poor re-expansion of upper lobe; had empyema with bronchopneumonia
	11/ 4/39	2 days	13.9	15.0	94.2	
	11/ 7/39	5 days	12.0	13.7	88.8	
	11/13/39	11 days	10.4	12.1	87.6	
	11/20/39	18 days	12.4	13.7	91.8	
	12/13/39	6 weeks	13.2	14.0	95.6	
	1/12/40	10 weeks	14.5	15.7	93.2	
B. T., aged 26; bronchiectasis, left lower lobe; previous left thoracoplasty for tuberculosis. Lobectomy, 6/26/41	7/ 1/41	5 days	12.8	14.6	88.7	Postoperative course satisfactory
	7/11/41	15 days	12.8	14.0	93.0	
J. V., aged 50; chronic pulmonary abscess. Partial left upper lobe lobectomy, 4/4/41	4/11/41	4 days	12.0	12.9	92.7	Postoperative course satisfactory except for small empyema

*Patient receiving oxygen at time of determination.

TABLE III

EFFECT OF BRONCHOCUTANEOUS FISTULA ON ARTERIAL OXYGEN SATURATION

FISTULA	ARTERIAL OXYGEN SATURATION (%)
Fistula open with patient breathing room air	87.2
Fistula closed with patient breathing room air for 45 min.	90.7
Fistula open with patient breathing 100 per cent oxygen for six min.	93.7
Fistula closed with patient breathing 100 per cent oxygen for 6 min.	96.7

DISCUSSION

After surgical intervention in the thorax, anoxic anoxia is frequently present. Whereas the value of oxygen therapy in major thoracic surgery has been well established, no data have been available to aid in determining how long the anoxia persisted following operation. It is usually customary to administer oxygen for only a few days after operation unless the patient is obviously dyspneic or cyanotic. Yet our studies have shown that in some patients in whom no dyspnea or cyanosis was present a significant degree of anoxic anoxia persisted for weeks. When oxygen therapy was again instituted in such instances, marked clinical benefit was observed.

A comparison of the arterial oxygen saturation after pneumonectomy with the values obtained after lobectomy reveals the unexpected finding that the anoxic anoxia was apparently often more pronounced and lasted longer after lobectomy than after pneumonectomy in the absence of postoperative complications. The explanation of this finding lies in the fact that after uncomplicated total pneumonectomy all the blood flows through the opposite lung, which is well ventilated. Following lobectomy, however, the remaining lobe or lobes on the operated side are frequently poorly ventilated for a time postoperatively. Even though the roentgenogram may show good expansion of the remaining lobe immediately after operation, the actual ventilation of that lobe may be poor. Since a considerable amount of blood may be flowing through the pulmonary vessels of the poorly ventilated lobe, arterial oxygen unsaturation results. Pulmonary collapse because of failure of the lobe to re-expand, or collapse caused by compression from pleural fluid, was a frequent finding in those cases which showed marked or prolonged anoxic anoxia after lobectomy.

Following pneumonectomy there were only two cases without postoperative pneumonia or empyema in which the arterial oxygen saturation did not return to a nearly normal level by the end of the first week after operation. In both of these instances there was a close correlation between the arterial oxygen saturation and a change in the position of the mediastinum. In one patient (E. B.) the mediastinum was displaced toward the remaining good lung by a large fluid accumulation on the operated side. Following withdrawal of the excess pleural fluid and return of the mediastinum to a normal position there was a prompt return of the arterial oxygen saturation to normal. In the other patient

(D. M.) the usual postpneumonectomy mediastinal deviation toward the operated side could not be tolerated because of the pulmonary emphysema present. Here again the arterial oxygen saturation returned to the preoperative level when the mediastinal displacement was lessened.

Longacre, Carter, and Quill[2] made an experimental study of some of the physiologic changes following total pneumonectomy in dogs. These authors did not study the animals in the early postoperative period but found little or no arterial oxygen unsaturation at rest two months after pneumonectomy. A severe exercise which had not caused anoxia before pneumonectomy resulted in marked arterial oxygen unsaturation after pneumonectomy. Longacre, Carter, and Quill quote Heuer and Andrus as having noted in resting animals "a marked fall in the blood oxygen content up to the eleventh day, returning to normal by the twenty-fifth to thirtieth day." These determinations by Heuer and Andrus[3] were made on venous and not arterial blood. It is not stated whether the venous blood was mixed venous blood from the right heart or whether the blood was obtained from a peripheral vein, although this would influence the results. Studies of the arterial oxygen saturation in the early postoperative period after pneumonectomy in dogs would not be applicable to man. When pneumonectomy is performed in a dog, a contralateral pneumothorax results and therefore the expansion of the opposite lung may be altered to a considerable degree immediately after operation. There are practically no data to be found in the literature concerning the degree and duration of anoxic anoxia which may occur in the early postoperative period after major thoracic surgical procedures in man.

The effect which a bronchial fistula will have on the oxygen saturation of the arterial blood may vary with the size of the fistula. The effect of a bronchocutaneous fistula may be less marked than that of a bronchopleural fistula because of the possibility of more rebreathing with the latter. A large bronchial fistula may interfere seriously with adequate ventilation of the lungs. Touroff[4] has reported a case in which fatal anoxemia resulted from a large bronchopleural fistula following pneumonectomy. His patient became dyspneic and cyanotic whenever the opening to the large fistula was not occluded by a packing. No determinations of the arterial oxygen saturation were reported in that case.

The oxygen saturation of the arterial blood was determined in a small number of cases after thoracic exploration. The operative procedures were performed chiefly for pulmonary tumors which proved to be inoperable. All of the cases showed a slight reduction in the arterial oxygen with the saturation varying from 89.5 to 93.0 per cent (Table IV).

The arterial oxygen saturation was also studied in twenty-seven patients after thoracoplasty. A slight reduction in arterial oxygen saturation was often observed even in some good-risk patients with no post-

TABLE IV

EXPLORATORY THORACOTOMY

CASE	TIME OF DETERMINATION	ARTERIAL OXYHEMOGLOBIN		
		CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)
R.B.	Preoperative	17.8	19.7	91.5
	4 days postoperative	15.6	17.2	91.7
H.G.	1 day postoperative	10.4	11.3	93.0
R.P.	Preoperative	15.3	17.0	91.0
	7 days postoperative	13.8	15.3	91.6
J.T.	Preoperative	16.9	18.4	92.7
	1 day postoperative	13.9	15.6	90.0
	5 days postoperative	13.0	14.7	89.5
R.Z.	Preoperative	16.1	17.3	93.4
	3 days postoperative	14.8	16.5	90.8

operative complications. Although most of the patients studied after thoracoplasty showed an appreciable drop in the per cent saturation of the arterial blood with oxygen, these findings do not give a true picture of the frequency of anoxia immediately following the thoracoplastic procedure. Not all of the patients subjected to thoracoplasty during a given period were studied but the investigation stressed rather the poor-risk group.

In order to determine whether the finding of postoperative anoxic anoxia was peculiar to thoracic surgery, a small group of patients who had undergone major abdominal surgery was studied as controls. In determinations of the arterial oxygen saturation of thirteen patients shortly after an abdominal operation, chiefly procedures in the upper abdomen, no instance of anoxic anoxia was found (Table V). None of these patients had any pulmonary complications but in some the diaphragm was elevated by abdominal distention. The patients were receiving morphine at the time the determinations were made.

TABLE V

ABDOMINAL CASES

CASE	OPERATION	DAYS POSTOPERATIVE	ARTERIAL OXYHEMOGLOBIN		
			CONTENT (VOL. %)	CAPACITY (VOL. %)	SATURATION (%)
M.B.	Cholecystectomy	1	13.2	13.9	96.3
F.D.	Cholecystectomy	1	12.7	13.4	96.1
M.B.	Cholecystoduodenostomy	1	13.8	14.7	95.1
W.K.	Cholecystectomy	1	18.4	19.8	93.8
J.K.	Gastrectomy	4	12.7	13.6	94.3
J.M.	Appendicectomy	2	19.6	20.9	94.4
J.S.	Gastrectomy	1	15.6	16.6	94.8
S.S.	Exploratory laparotomy	3	15.3	16.1	95.1
T.T.	Cholecystectomy	1	18.6	19.1	98.3
A.T.	Gastroenterostomy	1	13.0	14.1	93.8
J.T.	Laparotomy	1	14.7	15.7	94.6
E.W.	Cholecystectomy	1	11.4	12.2	94.4
M.H.	Exploratory laparotomy	2	12.9	14.1	93.0

It should be pointed out that a normal arterial oxygen saturation does not necessarily mean that oxygen therapy would be of no benefit. Although the saturation of the arterial blood may be within normal limits, the venous blood may have an abnormally low oxygen content and the tissues may not be supplied with adequate amounts of oxygen. The use of high oxygen concentrations may increase the oxygen content of the arterial blood above ordinary levels and thus be an aid in the treatment of stagnant anoxia.[5] Also, in spite of a normal arterial saturation, oxygen therapy may be indicated in stagnant anoxia for the purpose of reducing hyperventilation and decreasing whatever dyspnea is present.

Our present investigation has not included observations on the day of operation. The importance of avoiding anoxia during anesthesia and operation has received considerable attention recently. The importance of adequate ventilation and oxygenation during thoracic procedures cannot be overemphasized. Anoxia undoubtedly has been the main etiologic factor in many an instance of death during or shortly after a thoracic operation when the fatality was attributed to heart failure. Patients with pulmonary emphysema and fibrosis show the most marked disturbances in arterial oxygen saturation after thoracic surgery and even a relatively small intervention may cause considerable anoxia.

The effect of drugs which depress respiration must be considered in an evaluation of the causes of anoxia. During the early postoperative period the patients studied were receiving morphine and other sedatives. Generally the drugs were employed in small doses. The blood for analysis usually was not obtained in close relationship to the time when the sedative was administered. McClure and his co-workers[6] have reported anoxia after the administration of various sedatives and analgesics, but we do not believe that this is a significant factor in our results. The cases investigated after abdominal surgery were receiving similar doses of morphine at the time they were studied and did not show anoxic anoxia. Large doses of sedatives, however, may well be a factor in anoxia.

Determinations of the arterial oxygen saturation in the postoperative period after thoracic surgery have repeatedly demonstrated the inaccuracy of clinical criteria of anoxia. The unreliability of dyspnea and cyanosis as accurate signs of oxygen deficiency must be stressed. Severe anoxia may exist in the absence of cyanosis, especially if the patient is anemic. The importance of other signs and symptoms of anoxia, such as those seen at high altitudes, is frequently overlooked.

Our investigation permitted us to compare the presence of clinical signs or symptoms of anoxia with the arterial oxygen saturation. In a considerable number of cases there was no dyspnea in spite of anoxic anoxia. Cyanosis was often difficult to detect, sometimes because of pallor. A number of patients complained of headache and anorexia when the arterial oxygen saturation was below normal, and these symptoms, when caused by anoxia, were frequently relieved by oxygen ther-

apy. In one patient (A. F.) restlessness, mental confusion, and hallucinations with muscular incoordination were observed during marked anoxia. The cause of the symptoms was suggested by the determination of the arterial oxygen saturation. Instead of waiting for such symptoms of anoxia to develop, however, it is preferable to make a determination of the arterial oxygen saturation routinely. By this means the presence of anoxic anoxia will be detected in its earliest stages and indicate that the administration of an atmosphere rich in oxygen may be beneficial.

SUMMARY AND CONCLUSIONS

Studies of arterial oxygen saturation have been made, before and after operation, in 17 cases that had pneumonectomy and in 21 cases that had lobectomies. From the data obtained the following conclusions were drawn.

1. Unrecognized anoxia is a common occurrence in thoracic surgery, and not infrequently is of major importance.

2. Following lobectomy there was frequently some degree of anoxia for a week. The remaining lobe on the operated side re-expanded poorly in two cases and the anoxia was more prolonged in these instances.

3. Following total pneumonectomy in the good-risk patient without complications, the oxygen saturation of the arterial blood returned to a normal level within a few days of operation.

4. Complications in the postoperative period after lobectomy and pneumonectomy frequently resulted in anoxia.

5. Significant anoxia was sometimes present in the absence of dyspnea and cyanosis. Symptoms such as headaches, restlessness, and mental confusion encountered in the postoperative period were in some instances due to anoxia.

6. If complications arise after pulmonary resection, prolonged oxygen therapy may be indicated.

7. Determinations of the oxygen saturation of the arterial blood after thoracic surgery may reveal unsuspected anoxia, sometimes of severe degree. Since the technique is simple, arterial oxygen determinations should become a part of the management of patients after pulmonary resection.

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THE EFFECT OF ATROPINE ON GASTRIC SECRETION DURING THE NIGHT

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THERE have always been differences of opinion concerning the secretion of gastric juice during the interdigestive period. Spallanzani (1783) and Brown (1876) postulated that the secretion of gastric juice is continuous. Beaumont (1847) observed that the gastric juice was never found free in the unstimulated stomach of Alexis St. Martin. As early as 1895, Schnele studied the secretion and motility of the normal human stomach by means of a catheter left in situ. Pavlov (1910) and his pupils believed that, in the absence of secretory stimuli such as food, acting from the mouth cavity, stomach, or upper part of the small intestine and when certain "psychic influences" are also absent, the peptic glands remain in a state of rest under which condition no gastric juice is secreted.

Rehfuss, beginning in 1914, determined the previous conception of the fasting stomach to be erroneous by obtaining amounts of 30 to 120 c.c. of fasting secretion from healthy medical students. Carlson (1916) found that, in the absence of food or psychic factors, there was a continuous secretion of the gastric glands varying from 2 to 50 c.c. an hour with an average content of 40 c.c. of fluid in the fasting stomach. He observed that this continuous or "hunger secretion" had a uniformly lower acidity than the appetite juice. Crohn and Reiss (1917) believed that an "after secretion" might persist for many hours postprandial but they considered it a manifestation of pathologic hypersecretion; they were unable to duplicate the work of Rehfuss in normal individuals. Rehfuss and Hawk (1921) inferred that the gastric residua which they obtained were due to a constant secretion of the gastric glands which they believed to be continuously active. They found during the interdigestive period that the secretory rate, the free acidity, and the total acidity were all reduced. Lim (1924) considered the continuous secretion as the "basal secretion" of the stomach to which the subsequent enhanced activity of the glands, as a result of controlled stimulation, must be related. Chalfen (1928) and Henning and Norpoth (1933) reported that normal subjects did not have an acid secretion during the night in contradistinction to the secretion of a juice of high acid value by patients suffering from peptic ulcer. Winkelstein (1935) confirmed this work when he found that nine out of twenty normal patients showed no free acid secretion during the night, the remainder having very low values with a composite peak

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of 12° at eleven o'clock. He reported that the quantity of secretion seldom exceeded 15 c.c. during the whole night, whereas patients with peptic ulcer averaged high volume and acid values.

Hellebrandt and co-workers (1936) contrasted the diurnal and nocturnal responses of the same normal subjects. They found that, in general, the acidity of the gastric juice spontaneously liberated during sleep at night was higher than that produced during the day and postulated that if the stomach has the ability to liberate spontaneously a juice of high acid value, its nocturnal responsiveness exceeds that of the day.

Sandweiss (1941), in studying gastric secretion at night in both normal individuals and peptic ulcer patients, reports that he obtained secretory volumes in both groups much higher than previously reported. He found the volume of secretion significantly higher in ulcer patients although the concentration of free acid was about the same in both groups.

Many theories have been postulated to explain the mechanism of interdigestive gastric secretion. It has been attributed to the mechanical irritation of the tube or a result of psychic influences producing a secretion via the vagus nerve. Carlson believed that the products of the autodigestion of the mucin and proteins in the gastric juice yielded gastric secretagogues which act as chemical stimuli for a slow continuous gastric secretion. However, Hellebrandt has pointed out that continuous aspiration affords minimal opportunity for this to take place. The whole problem was reviewed by Babkin (1932), who advanced the view that continuous gastric secretion is always due to the action of normal or abnormal stimuli among which he listed conditioned reflexes, the swallowing of saliva and regurgitation into the stomach of duodenal juices, food residuum in the stomach, food masses in the intestine, skin disease or infection, and the presence of gastric gases. Hellebrandt, in emphasizing the cyclic nature of the production of acid, postulates that gastric secretion, like gastric motility, is augmented during sleep at night, the secretory and motor mechanisms of the stomach being similarly governed.

The importance of thoroughly comprehending the nature of the interdigestive gastric secretion is readily realized when the role of acid in the production of peptic ulcer is considered. The occurrence of ulcer only in those individuals whose stomachs secrete free hydrochloric acid; the hypersecretion of gastric juice in ulcer patients (particularly duodenal ulcer); the occurrence of ulcer only in those parts of the gastrointestinal tract exposed to the action of gastric juice; the occurrence of ulcer in Meckel's diverticulum adjacent to patches of ectopic fundus mucosa; the absence of recurrent ulcer in patients exhibiting achlorhydria after gastrectomy; the success of medical management of ulcer when based on the principle of neutralization of the free acid; experimental ulcer production when gastric secretion impinges on a mucosa unprotected

by alkaline duodenal secretion, and the experimental production of ulcer in laboratory animals after the injection of histamine in beeswax—all these occurrences contribute to accumulated evidence that acid gastric juice is the sine qua non of ulcer. Thus, it is believed highly probable that during the interdigestive phase the acid gastric juice, undiluted by other secretions and unmixed with diluting, adsorbing, and neutralizing foodstuffs may be harmful to the mucous membranes. Whether the hypersecretion and hyperchlorhydria during the night are cause or effect, it is fair to suspect that the acid gastric juice is responsible for the initiation of the lesion, for its extension, and for its chronicity.

There have been many attempts to control gastric secretion by the administration of pharmacologic products. Atropine and related compounds, because of their effect on the parasympathetic nervous system, have been extensively used. The regulatory activity of the vagus nerve on gastric acid secretion is an established fact but the influence of the splanchnics is still open to question. Bickel (1925) believed that the sympathetic nervous system had the major role in the production of enzymes by the gastric glands whereas the parasympathetic nervous system played a secondary part, influencing chiefly the secretion of water and acid. Baxter (1934) has shown that the sympathetic nervous system has some relation to the secretion of mucoid fluid by the gastric mucosa. However, it has never been definitely demonstrated that the sympathetic nerves directly influence the activity of the peptic or parietal cells.

The site of action of atropine is usually considered to be on the postganglionic nerve endings in the cells or neurocellular substance but the subject is not clearly settled. Gray and Atkinson have suggested that, since atropine does have some effect on the secretory response to histamine, it must act on the cell as well. Ivy advanced the suggestion that atropine may prevent the formation of the secretory hormone in the stomach.

Since atropine depresses the parasympathetics, one would expect it to depress or completely inhibit the primary or cephalic phase of gastric secretion, which is a reflex transmitted to the stomach via the vagus nerve. In laboratory animals it has been found that the secretion of appetite juice may be abolished by atropine. In human beings, Rehfuss found that $\frac{1}{50}$ gr. atropine, given hypodermically, reduced this secretion but did not abolish it. The intestinal phase of gastric secretion is, according to Ivy, mediated by the vagi and in laboratory animals is diminished or abolished by large doses of atropine. There have been no reports of the effect of atropine upon this phase in human subjects.

What atropine does to the gastric or chemical phase, however, is not clear. The vagi also seem to be concerned in the mechanism of this phase for Orbeli (1906) has demonstrated that after their section this secretion is diminished. Klein (1933) has shown that in dogs atropine

can abolish the secretion due to chemical stimuli in the stomach in transplanted pouches deprived of all peripheral nerve supply and subject only to humoral influences. In man, however, some (Pokras and Michelson) believe that this phase cannot be suppressed although Bastedo states that doses large enough to cause toxic reactions may inconstantly bring about a distinct reduction in the amount of secretion and acid titer. It should be borne in mind, however, that the gastric phase is given its start by the chemical substances formed from food by the action of psychic juice; thus, it is possible that if the appetite juice is diminished, the chemical juice will be developed more slowly.

Many other investigators have extensively studied the effect of atropine on gastric secretion. All who have observed its effect in animals agree that secretion is checked in all of its normal phases. Keeton (1933) found that in the dog the first effect of atropine is to decrease total quantity of both the gastric secretion and the pepsin content whereas the acid concentration is not decreased until a sufficient amount of atropine has been given to reduce the total quantity of secretion to an amount approximately 20 to 50 per cent of its original volume. Atkinson and Ivy (1938) confirmed these results, obtaining a volume reduction of 50 per cent in the response of the Pavlov pouch secretion to histamine with a diminution of 66 per cent in the total acid output as measured in milligrams. Bastedo suggested that these results could only be expected with the large doses of atropine that can be given the experimental animal.

However, there exist wide differences of opinion concerning the effect of atropine in man. Porter (1932) observed that the height reached by the free acidity was not affected by atropine but that the volume was definitely decreased, the reduction varying from 40 to 60 per cent. Keefer and Bloomfield (1926) and Atkinson and Ivy (1936) obtained similar results, the former reporting a marked diminution in the total quantity of secretion as well as a reduction in the acidity without parallelism in the degree of reduction of each. Atkinson and Ivy, studying the effect of atropine and its derivatives on the gastric secretion of ulcer patients, concluded that there was no effect on the height of the titratable acidity but that the volume of secretion was diminished in comparison with the control. To obtain this effect, they found it necessary to administer doses of artopine large enough to produce untoward side reactions.

Lockwood and Chamberlin (1922) found that maximal chemical dosages of atropine depressed both the free and total gastric acidity about 30 per cent. Bolton (1923) and Roberts (1925) confirmed this observation; all believed that the attendant relaxation of the pyloric sphincter associated with the regurgitation of the alkaline intestinal fluid, as indicated by the earlier appearance of bile in the samples and by the sudden or gradual rise of the inorganic chloride curve, allowed neutralization to occur earlier or more frequently.

Kalk and Siebert (1927), Polland (1930), and Klumpp and Bowie (1933) reported that the volume of secretion was reduced after atropine but that the free acid values were higher. Polland attributed the rise of titratable acidity to the relatively slight inhibitory effect of atropine upon the total output of acid with a consequent increase in the amount of acid per cubic centimeter of gastric content.

Crohn (1918) was unable to produce any reduction in gastric acidity by the use of atropine. Winkelstein (1933) obtained equivocal results. Palmer (1933) and Bastedo (1936) observed that atropine diminished the volume and acidity of gastric secretion but only in quantities sufficient to produce other unpleasant physiologic effects. The effect on gastric secretion was short lived while the toxic manifestations persisted for longer periods. In doses permissible for continuous therapy, they found that belladonna and atropine were practically without effect on the secretory and motor functions of the stomach. Bastedo emphasized that frequently the reduction in the volume of secretion is associated with a much smaller proportionate reduction in the total acid secreted resulting in a more strongly acid solution than normal with consequent increased irritant action. Doses large enough to reduce acid secretion were also found to reduce the secretion of protective mucin.

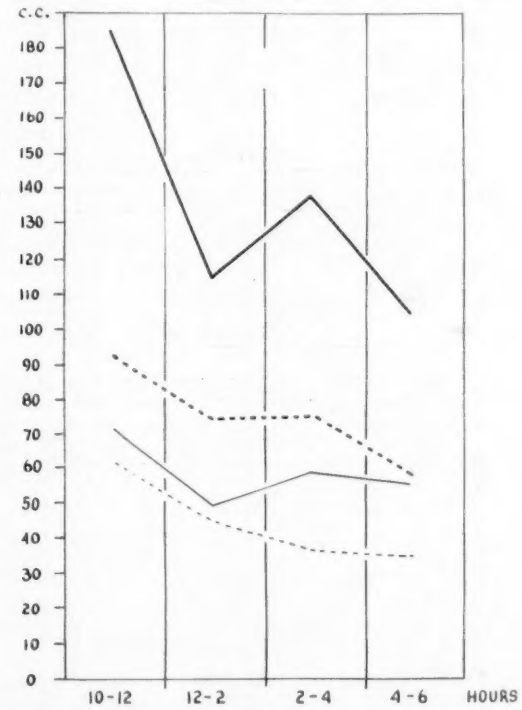
There are many others who have reported the reduction of gastric acidity by the administration of physiologic doses of atropine. Riegel (1899) found that atropine caused a decrease of free and total acid after a test meal of one liter of milk. Moore and Kilroe (1910) reported a reduction averaging 13.6° for free acid and 13.10° for total acid after the administration of belladonna by mouth. Mathieu and Roux (1914) considered atropine the most useful drug at their disposal for cases of hypersecretion. Schmidt (1914) believed that atropine diminished the secretion of the gastric glands and advocated its use in hyperacidity. Bennett (1921) found consistent diminution in gastric acidity after the administration of therapeutic doses of oral atropine. Schuff (1900), Bergman (1913), Chiari (1915), Hernando (1923), Kilterman (1925), Roll (1926), and Loeper and Fau (1933) may be listed among the many others who agree that atropine is effective in reducing gastric acidity.

The question as to why so many divergent results have been reported concerning the effect of atropine on gastric secretion has frequently been raised. Atshuler (1928) attempted to reconcile contradictory observations on the basis that the action of the drug depends upon what phase of activity the cells are in when the stimulus reaches them. He believes that the same drug acting on the same cell might at one time result in stimulation and at another in inhibition. However, it is probable that most of the inconsistencies are due to differences in atropine dosage and method of administration, different types of stimuli used to induce secretion (test meals, alcohol, histamine), duration of test period, time relationships relative to the administration of atropine, and

differences in criteria used for determining inhibition of secretion. The reason for the difference in atropine action between man and dog is unknown. Klein postulates that one cause may be that more of the humoral stimuli act directly on the cell in man; in this case atropine would be relatively less effectual.

METHOD

Observations were made upon fifty University Hospital patients who presented no evidence of gastrointestinal disease other than chronic cholecystitis[15] and recurrent appendicitis in the interval phase.[11] In addition, fifteen patients with active duodenal ulcers were studied.



	NORMAL		ULCER	
HOUR	CONTROL	ATROPINE	CONTROL	ATROPINE
10-12	71·3	61	184·7	92·5
12-2	48·5	46·8	116·1	75·9
2-4	58·1	37·4	139·1	76·3
4-6	55·7	35·8	104·8	59

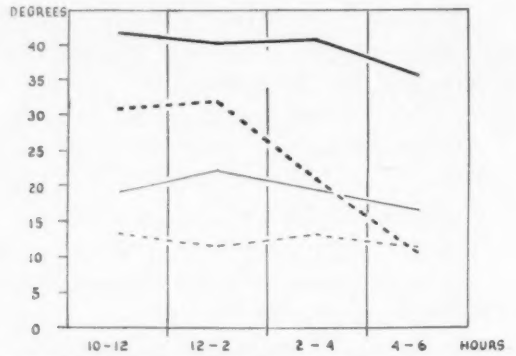
KEY
NORMAL - CONTROL
NORMAL - ATROPINE
ULCER - CONTROL
ULCER - ATROPINE

Fig. 1.—Graph showing volumes of gastric juice secreted at night by fifty normal and fifteen ulcer patients (average values).

The average age of the group selected as normal was 41.4 years, the youngest patient being 16 years, the eldest 75 years. Thirty were female, twenty male. In the ulcer group, thirteen were male, two female. The average age was 45.6 years with the youngest 29 years, the eldest 64 years.

The method of study of the patients in each group was identical. Each patient was studied on two successive nights, the first night serving

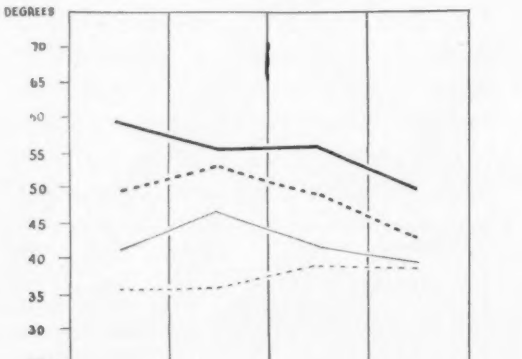
as a control and atropine being given on the second. The usual hospital meals were served on each of the days preceding the test, the five o'clock dinner consisting of soup, meat, potato, vegetable, and dessert. Duodenal tubes were inserted through the nose into the stomach at seven o'clock, no lubricant being used and suction siphonage instituted



HOUR	NORMAL		ULCER	
	CONTROL	ATROPINE	CONTROL	ATROPINE
10-12	19·2	13·7	42·8	30·9
12-2	22·4	11·9	40·2	32·4
2-4	19·3	13·6	40·9	20·8
4-6	16·5	12·1	35·4	10·8

KEY
NORMAL CONTROL
NORMAL ATROPINE
ULCER CONTROL
ULCER ATROPINE

Fig. 2.—Graph showing free acidity of gastric juice secreted at night by fifty normal and fifteen ulcer patients (average values).



HOUR	NORMAL		ULCER	
	CONTROL	ATROPINE	CONTROL	ATROPINE
10-12	40·7	35·3	59·7	49·6
12-2	46·4	36·1	59·1	53·1
2-4	42·6	38·4	55·4	49·2
4-6	39·4	38	49·8	43·2

KEY
NORMAL CONTROL
NORMAL ATROPINE
ULCER CONTROL
ULCER ATROPINE

Fig. 3.—Graph of total acidity of gastric juice secreted at night by fifty normal and fifteen ulcer patients (average values).

directly. At nine o'clock, 2 gr. sodium luminal were given hypodermically; this was repeated in five hours if the patient was still awake. No fluids were allowed after nine o'clock. No attempt was made to aspirate the salivary secretion.

At ten o'clock the returns from the suction were discarded, following which collection was made of the gastric secretion at intervals of two hours during the night. On the second night, the procedure was identical except for the administration of $\frac{1}{75}$ gr. atropine sulfate dissolved in 120 c.c. of tap water by proctoclysis at 10 P.M., 1 A.M., and 4 A.M., using a continuous drip adjusted to a rate of four drops a minute.

The volumes of each of the two hourly returns were measured and the free and total acidity determined using. Toepfer's solution and phenolphthalein as indicators. No accurate notations were made regarding the presence of food particles, bile, blood, etc. in the samples.

RESULTS

The results are graphically recorded in Figs. 1, 2 and 3. The normal group presented a mean secretory rate of 29.3 c.c. per hour in contrast to the average of 68 c.c. per hour in the control ulcer series. With the use of atropine there was a mean decrease in the volume of secretion, free and total acidity as shown in Table I.

TABLE I

	NORMAL GROUP	ULCER GROUP
Volume	53 c.c. (22.6%)	60 c.c. (44.2%)
Free acid	5° (34%)	16° (40.4%)
Total acid	5° (12.4%)	6° (11.1%)

TABLE II

EFFECT OF ATROPINE ON THE NIGHTLY SECRETION OF GASTRIC JUICE STUDY OF 50 NORMAL AND 15 ULCER PATIENTS

	NORMAL 50 CASES			ULCER 15 CASES		
	VOLUME	FREE ACID	TOTAL ACID	VOLUME	FREE ACID	TOTAL ACID
Significant decrease (>20%)	25	24	20	12	10	8
No change (±20%)	13	14	15	1	3	4
Significant increase (>20%)	12	12	15	2	2	3

Table II represents an evaluation of the effect of atropine upon each individual studied. The net change for the period of 10 P.M. to 6 A.M., following the administration of atropine, in volume, free and total acidity of gastric juice secreted was calculated for each patient; a significant increase or decrease was considered as a variation from the control of more than 20 per cent.

Of the twenty-four cases in the normal series showing a significant decrease in the amount of free acid after atropine administration,

eighteen had no free acid in two or more of the two-hour periods and nine had no free acid in all four of the two-hour periods. Five patients in the ulcer group were achlorhydric in all specimens after the administration of atropine.

The only untoward side action to atropine noted was a dryness of the mucous membranes of the nose and throat of which the majority of the patients complained. Tachycardia exceeding 100 was present on only five occasions. No patient exhibited cerebral symptoms from the administration of the drug.

SUMMARY

1. The nightly gastric secretion of fifty normal and fifteen ulcer patients was studied on each of two successive nights, the first night serving as a control, with atropine being given by proctoclysis the second night.

2. In the control period, mean values indicate that the secretory rate, volume of secretion, free and total acidity are higher for the ulcer group. Atropine diminished the volume of secretion as well as the free and total acidity in both the normal and ulcer series. The decrease in these values was more pronounced in the ulcer group.

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ENDOMETRIOSIS: CLINICAL AND THERAPEUTIC CONSIDERATIONS

With a Report of 120 Private Cases

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ENDOMETRIOSIS, after more than twenty years of fairly intensive investigation, still holds the unabated interest of physicians and surgeons, for several reasons. Its etiology remains largely a matter of speculation, its pathologic and clinical manifestations continue to defy recognition, and the proper methods of its treatment are still disputed. Further, the condition is far more prevalent than the profession in general yet realizes. Chiefly responsible for this fact, no doubt, is its common association with adenomyosis and other pelvic diseases; the surgeon is easily deceived into attributing the patient's symptoms to one or more of these disorders and overlooking entirely the possibility of endometriosis.

Believing that a fuller appreciation of the true incidence of endometriosis can be gained, and that some of the problems involved can best be clarified by reports of individual experiences and studies of selected cases, I will discuss the clinical and therapeutic features of the condition as I and others have observed them, and will follow this with a critical review of my own cases treated within recent years.

Opinion regarding the mode of origin of endometriosis is divided chiefly between two theories: one, that of Sampson,[9] that the masses develop from bits of müllerian mucosa deposited on the peritoneum by retrograde menstrual flow; that they either remain superficial or invade and contract the underlying structure; and that, after invading the ovary, they enlarge and give rise to a cyst, which ruptures and in turn disperses other implants over the pelvic structures. According to the second theory, suggested by Ivanoff,[5] the process develops by metaplasia of celomic epithelium. Still another possibility was advanced by Cullen[2]: that the endometrial tumors grow from embryonic rests of müllerian tissue. In any event, it is generally believed that the basic factor is a glandular imbalance which results in overactivity of the hormones, and, further, that this influence often continues in the ectopic endometrium, causing it to enlarge and recede with each menstrual period.

Just when this hormonal activity begins to incite the pathologic process is likewise a matter of conjecture. Some authors believe it begins with the onset of menstruation, or soon thereafter, and progresses slowly over a period of years. This may be true of cases in which the

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uterus is not involved; it is questionable, however, whether it applies to those wherein benign uterine disease is associated, although the latter also is believed to be activated by glandular hyperfunction. It has been our observation, and that of others as well, that adenomyosis usually develops in older women.

The reason for the later appearance of tumors of the uterus may lie in the structure of the organ, which may possibly prevent their early manifestation. Yet, this does not fully explain the difference. Dreyfuss,[3] among others, has suggested that multiparity may be one factor in uterine tumors, the sterility index being lower than normal in the lower age group. Meigs[7] is of the opinion that the appearance of endometriosis, on the other hand, may be favorably influenced by late marriage and contraception, in that hormone function is unrelieved by the physiologic rest afforded by pregnancy. Could the difference be one of origin? The theory of metaplasia of celomic epithelium might best apply to endometriosis without uterine disease, especially since patients so affected fall in the younger age groups.

This thought leads to a consideration of the role of sterility in endometriosis. Since both sterility and endometriosis are evidence of glandular imbalance, it is conceivable that they are coincident features of the same disturbance rather than, as some authors believe, that sterility is an active agent in the disease process. This would seem to be true whether the endometriosis develops in a nullipara, the sterility in this case being primary, or whether symptoms present themselves following one or more pregnancies, the sterility then being secondary.

The frequent association of retroversion with endometriosis has given rise to the opinion that this condition may also be a contributing influence. I am convinced, however, that, with few exceptions, the retroversion in these cases is caused by puckering and consequent shortening of the uterosacral ligaments by the implants, or by fixation of the uterus to the sigmoid by adhesions incident to implants between these two structures.

Pathology.—In the majority of cases, external endometriosis involves one or both ovaries, and the pelvic peritoneum as well. In the ovary, it is usually present in the familiar chocolate cyst, though fragments of endometrial tissue are occasionally found in hemorrhagic and other types of ovarian cysts. Outside the ovary, the implants may be widespread over the pelvic floor and on the pelvic wall, or may be scattered at only a few points. The most common site is the posterior wall of the uterus, the uterosacral ligaments and the sigmoid also being involved. Generally, in such cases, the uterus is drawn backward and is attached to the sigmoid, and the whole constitutes a fixed mass. Often, extensive deposits are distributed along the sigmoid or rectum. Other common locations are the bladder fold of the peritoneum and anterior wall of the uterus and cervix, rectovaginal septum, and broad ligament. Rarely, endometrial tissue is found in the inguinal region, in the

perineum, on the small bowel, appendix, and abdominal wall, and in the omentum, umbilicus, lungs, and laparotomy scars.

Whether deposited primarily through the tubes or secondarily from perforated cysts, as Sampson believes, or whatever their origin, the implants tend to incite an inflammatory reaction and adhesions in the adjacent structures; thus, at operation, one may observe an acute, widespread peritonitis, all the pelvic organs being bound together in an almost impenetrable mass of adhesions. This process, incidentally, explains many inflammatory conditions of the pelvis for which formerly no cause could be assigned.

Symptoms.—The cardinal features of peritoneal endometriosis are menstrual irregularity and pelvic pain. The menstrual disorder is usually a menorrhagia or metrorrhagia, though some patients have only a spotting between periods, or even amenorrhea. The pelvic pain may be general, or localized to one side or another, or it may be referred to the back or down the thighs. Referred pain is especially significant, indicating, usually, a penetrating lesion or one which has incited an inflammatory reaction. Again, the pain may be severe, or may be described as a drawing sensation, or merely a soreness, tenderness, or discomfort in the pelvis. The intensity of the pain is believed to be governed by the function of the implants under hormonal influence. The more severe pain may be acute in onset, resembling that of acute appendicitis or an acute intestinal obstruction. The milder types are usually chronic, covering a period of months or years.

Not all patients, however, have either menstrual disturbance or pain. Rather, many of them complain of symptoms referable to the gastrointestinal or urinary tract, a vaginal discharge, nervousness, loss of appetite and weight, headache, and dyspareunia. A few come to the physician solely because of an abdominal mass. Others seek examination because of sterility. When such conditions are accompanied by abnormal menstruation and low abdominal pain, they afford additional evidence of endometriosis; alone, however, they may present a confusing and entirely misleading picture which cannot be clarified except by a thorough pelvic examination and more often than not, not even then. Especially is this true of younger women in whom the process is not well advanced.

Diagnosis.—The most reliable diagnostic measure is rectovaginal examination. By this means, fixed, painful, nodular masses in the uterosacral ligaments, in the cul-de-sac, or on the rectovaginal shelf may be readily detected, and when present, may be regarded, practically without doubt, as endometriomas. Similarly, retroversion and uterine tumors and ovarian cysts may also be palpated. If adhesions are extensive, however, the different organs may be indistinguishable, and individual areas of endometriosis impossible of delineation.

Especially significant in the diagnosis is the fact that symptoms are exaggerated during menstruation. Not infrequently, this feature is the

only clue to the nature of the disease. Indeed, the patient may have no difficulty whatever except at the menstrual period. An illustration of this fact is found in tumors of the broad ligament or abdominal wall, which manifest themselves solely by local tenderness and swelling at menstruation.

Primary invasion of the sigmoid or rectum probably presents the most serious of the diagnostic problems associated with endometriosis. Although deposits are frequently found in these areas as a part of a general pelvic distribution, they seldom involve the colon wall to such an extent as to give rise to symptoms, and a primary endometrioma is even more rare.

Signs of obstruction, the palpation of a mass posterior to the uterus, and the proctoscopic finding of a puckered area in the lumen of the bowel without an appreciable reaction in the surrounding tissues are fairly definite proof of the endometrial nature of the growth. The roentgenographic demonstration of a lesion is useful, but cannot be relied upon for a differential diagnosis.

Occasionally, however, without any definite warning, one is confronted at operation with a growth in the sigmoid or rectum which simulates cancer and is entirely unaccompanied by other areas of endometriosis. Unless one is familiar with the clinical characteristics of such lesions, the patient is likely to be subjected to a colon resection on the diagnosis of malignancy. A case is reported herein, in which this was done, several years ago. The most significant point in the diagnosis is the fact that endometriomas of the colon, as of other regions, are manifested by the usual menstrual symptoms.

Treatment.—The treatment of endometriosis is, in my opinion, entirely surgical. If the implants are extensive, involving both ovaries, all the pelvic organs should be extirpated. When only one ovary is affected, however, and all the peritoneal implants are removable, the good ovary may be left undisturbed. In young patients who complain of dysmenorrhea, a presacral resection may be performed in conjunction with a conservative operation, to prevent recurrence of the pain in the event of persistent endometriosis. The principal question in any case is not the patient's age, but the relief of symptoms and prevention of further damage and perhaps serious consequences, by interruption of the disease. If this can be accomplished without completely destroying ovarian function, well and good; if not, the radical operation should be carried out. The only exceptions are encountered in those patients at or near the menopause, whose symptoms are mild and in whom the disease may be expected to subside with the cessation of menstruation. In all other cases, the process is likely to cause trouble so long as ovarian function continues.

When the sigmoid or rectum is invaded, it may be advisable to resect the growth by an elliptical incision, in addition to oophorectomy. Partial resection of the colon is unnecessary; according to our experience, the growth will regress following removal of the ovaries.

The greatest difficulty in making a decision as to the best course to pursue is encountered when these patients present themselves for examination because of sterility. The slight possibility of subsequent pregnancy, despite preservation of the reproductive function, hardly compensates for the dangers of erring on the side of conservatism. Thirty-one per cent of a group of patients reported by Dreyfuss[3] were sterile, and Counseller[1] found an absolute sterility of 32.1 per cent of patients at the Mayo Clinic.

The use of radium or x-ray therapy in endometriosis seems hardly justifiable. In the first place, the risk to life is not a serious consideration in the choice of treatment, since the mortality from surgery is negligible. In the second place, there is almost invariably some associated disease which irradiation cannot relieve, and, in this event, radium is likely to give rise to infection and pelvic abscess. Or, if a sufficient amount of irradiation is given to destroy ovarian function, the uterus will be materially damaged. Further, the climacteric, with all its unpleasant manifestations, follows irradiation just as surely as it follows extirpation of the ovaries, yet all the diseased structures remain in the pelvis. Certainly, irradiation should never be given until the abdomen is opened, and then not until the presence of endometriosis is definitely proved by thorough exploration. An exact diagnosis is impossible without laparotomy.

I have collected a series of 120 cases of pelvic endometriosis discovered at operation within the past six years. These have been taken from our private clinic records and are therefore believed to give a fairly accurate picture of the incidence of the disease among surgical patients. The study does not include those with hemorrhagic or other types of ovarian cysts than the chocolate endometrial variety. Nor does it include adenomyosis unless associated with endometriosis, since a pathologic study was made of relatively few uterine specimens removed during this period. Moreover, in view of the more serious surgical considerations involved, our interest has been primarily in endometriosis.

The 120 cases of this series were encountered in a total of approximately 700 laparotomies for gynecologic diseases carried out during the same period, representing an incidence of 17 per cent. One hundred and four of the patients were married. The ages ranged from 17 to 53 years, the average being 38 years. Two were under 20 years; 19 between 20 and 30; 45 between 30 and 40; 49 between 40 and 50; and 5 beyond 50. Of the entire group, chocolate endometrial cysts of the ovaries were found in 83 (69 per cent) patients, and cysts of questionable endometrial origin and of other types were found in an additional 14. The endometrial process involved the peritoneum and other extra-ovarian structures in 106 (89 per cent). The distribution of the lesions and associated pathology is shown here.

Ovarian endometriosis, 83 (bilateral, 50; unilateral, 33)
Peritoneal endometriosis, 106

Abdominal endometriosis, 5 (omentum, 3; cecum 1; appendix, 1; abdominal wall, 1)
Associated benign disease of uterus and cervix, 84
Associated cancer of uterus, 1
Associated cysts of ovaries other than endometrial, 14
Associated hydrosalpinx, 5
Displacements of uterus, 41 (retroversion, 39; prolapse, 2)
Sterility, 24 (23 per cent of 104 married patients)

As shown above, the endometrial cysts of the ovary were bilateral in 50 cases and unilateral in 33. In 12, the endometriosis was confined to the ovaries alone, whereas in 23 it was limited to the peritoneum and other extraovarian structures. Peritoneal implants and cysts of the ovaries, endometrial and otherwise, were found together in 81 cases. Benign disease of the uterus and cervix was associated in 83 cases, and cancer of the uterus in 1, the 84 cases representing 70 per cent of the total. Other surgeons have reported a similar incidence of uterine and cervical disease.

The relative incidence of endometriosis and disease of the uterus and cervix in the different age groups is shown in Table I.

TABLE I

INCIDENCE OF ENDOMETRIOSIS AND DISEASE OF UTERUS IN 120 PATIENTS IN DIFFERENT AGE GROUPS

	UP TO 20		20 TO 30		30 TO 40		40 TO 50		50 AND OVER	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Endometriosis alone (36 patients)	2	6	12	33	17	47	5	14	0	
Endometriosis and uterine disease (84 patients)	0		7	8	28	33	44	53	5	6
Total	2		19		45		49		5	

The average age of those with external endometriosis alone was 31.5 years, and of the second group, 41 years. This finding conforms to that of other surgeons, that uterine disease develops later than endometriosis.

Five patients had previously had one ovary and tube removed, 23 had had an operation on the cervix or vagina or a curettage, 3 a shortening of the ligaments, and one a presacral neurectomy for dysmenorrhea.

The series was also reviewed with the idea of determining whether any relationship might exist between the ages of the patients and the extent and severity of the disease. The endometrial process was regarded as mild in 41 cases and severe in 79. The number and ages of the patients with each type are shown in Table II.

Contrary to the experience of some authors, we did not find more severe or more extensive endometriosis in the younger patients. Approximately 80 per cent of those with the severe type, and 75 per cent

TABLE II

INCIDENCE OF MILD AND SEVERE ENDOMETRIOSIS IN 120 PATIENTS IN DIFFERENT AGE GROUPS

AGE GROUP (YEARS)	MILD ENDOMETRIOSIS		SEVERE ENDOMETRIOSIS	
	PATIENTS		PATIENTS	
	NUMBER	PER CENT	NUMBER	PER CENT
Up to 30	8	20	13	16.5
30 to 40	14	34	31	39
40 to 50	17	41	32	40.5
50 and over	2	5	3	4
Total	41		79	

with the mild type were between 30 and 50 years of age. Twenty per cent of those with a mild endometriosis and 16.5 per cent with the severe degree were under 30 years of age.

The uterus was retroverted in 39 patients and prolapsed in 2. Of the total of 41, uterine disease was associated with the endometriosis in 20 cases, and in 21 endometriosis was present alone. As shown in Table I, 36 patients of the entire series had endometriosis without disease of the uterus; the incidence of 21 retroversions in the group of 36 therefore represents 58.3 per cent. The 20 patients with retroversion and both endometriosis and uterine disease constituted 24 per cent of the total number of 84 patients in whom the combined conditions were found. Thus, comparatively, retroversion was present with endometriosis alone in more than twice as many cases as retroversion with both endometriosis and disease of the uterus and cervix. Of the group of 21, there were 15 under 35 years of age, whereas in the group of 20, only 2 were under that age.

Twenty-eight of the 104 patients who were married had never borne children; 4 of this number, however, reported having one or more miscarriages. Nine of the 28 had retroversion, the uterus being bound in malposition by adhesions in every case. The only 4 of the 28 who might possibly have borne children, having one good ovary and an otherwise normal uterus, were among those with retroversion.

The symptoms as described by the total number of 120 patients were classified as follows:

Dysmenorrhea, backache, referred pain, 45
Pelvic pain and discomfort, 41
Menstrual disorders, 59 (Menorrhagia, 53; irregularity, 2; menopause, 4)
Miscellaneous, 61 (Gastrointestinal disturbance, cystitis, headache, nervousness, vaginal discharge, abdominal mass, dyspareunia)
Indefinite or no symptoms, 3

Counseller[1] has observed that menorrhagia usually is associated with chocolate cysts, and dysmenorrhea and referred pain with uterine and peritoneal endometriosis. We were unable to establish a connection between menorrhagia and dysmenorrhea or referred pain, respectively,

and the pathologic condition as it involved the ovaries, uterus, and peritoneum. Forty of the 55 patients with menorrhagia and irregular menstruation had some disease of the uterus, and 42 had peritoneal endometriosis. Three had peritoneal endometriosis alone, neither the uterus nor ovaries being affected. In only one patient with menorrhagia was the endometriosis limited to the ovaries; on the other hand, 14 who complained of menorrhagia had neither chocolate cysts nor any other disease of the ovaries.

Of the 45 patients with dysmenorrhea, 34 had cysts of the ovaries, 28 had some disease of the uterus, and the peritoneal and other structures were involved in the endometrial process in 41. Eleven patients with dysmenorrhea also had retroversion, and 10 of this number had pelvic endometriosis.

Forty-one patients described a low abdominal pain, pelvic discomfort, or pressure sensation which was apparently unrelated to menstruation. Thirty gave a history of gastrointestinal symptoms, 3 of this number having no other complaint. The sigmoid was involved in 10 of the 30, but could not be held entirely responsible for the symptoms because of associated disease of the appendix. Symptoms referable to the bladder were reported by 9 patients, 13 complained of a vaginal discharge, 11 of headaches, 3 of dyspareunia, and 11 were aware of a pelvic mass.

TABLE III

DURATION OF SYMPTOMS IN 120 ENDOMETRIOSIS PATIENTS IN DIFFERENT AGE GROUPS

AGE GROUP (YR.)	UP TO 1 YR.	1 TO 2 YRS.	3 OR MORE YRS.	NO SYMPTOMS	UNKNOWN
Up to 30	13	4	3	0	0
30 to 40	21	5	16	1	1
40 to 50	22	15	9	2	3
50 and over	1	2	2	0	0
Total	57	26	30	3	4

In Table III is shown the duration of symptoms as reported by the patients in each age group.

The duration of symptoms was recorded in 116 cases. Three patients had no symptoms. Of the 116, 83 (70 per cent) had had symptoms less than three years, 17 (20 per cent) of the 83 being under 30 years of age, 26 (31 per cent) between 30 and 40, 37 (45 per cent) between 40 and 50, and 3 (4 per cent) beyond 50. It is noteworthy that some of the younger patients had suffered for years, whereas some of the older ones had had symptoms for only a few days or few weeks.

A study of the duration of symptoms in the mild and severe types, respectively, revealed nothing important. As would be expected, in the majority of cases, the symptoms were of longer duration in the severe type. Some of the milder cases, however, including those wherein no endometrial deposits were found outside the ovary had produced symptoms over a long period of time, while a number wherein the deposits

were widespread were first manifested by an acute attack of a few hours' to a few days' duration.

A preoperative diagnosis of endometriosis was made in 29 (24 per cent) of the cases. The operations performed were as follows: Bilateral salpingo-oophorectomy, 97 (in 4, a portion of the ovary was transplanted); unilateral salpingo-oophorectomy, 20 (including 5 patients who previously had a salpingo-oophorectomy); hysterectomy, 109; shortening of ligaments, 6; presacral nerve resection, 1. Ovarian function could be preserved in 9 of the 11 whose uterus was undisturbed.

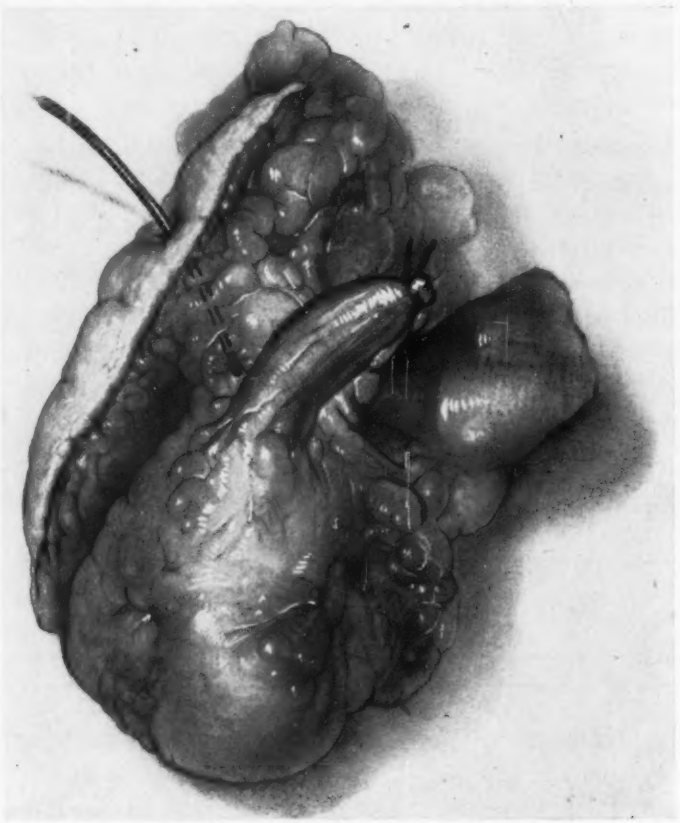

Fig. 14.—Inguinal endometrioma of round ligament, 2 by 3 inches, with sinus through which patient menstruated each month.

I have never had a patient die from operation for endometriosis. Four of the present group have not been heard from since leaving the hospital. Of the other 116, 112 were completely relieved by the operation, 3 were only partially relieved, and 1 has had a recurrence of the dysmenorrhea from which she suffered prior to operation. One of the patients who was only partially relieved was a girl, aged 19 years, for whom a presacral neurectomy was performed, the pelvic organs being undisturbed because of her age and the mild degree of endometriosis. Another was a young unmarried woman, aged 28 years, who had a subtotal hysterectomy and unilateral salpingo-oophorectomy. The third

was a married woman, aged 31 years, who had a total hysterectomy and unilateral salpingo-oophorectomy. The patient whose symptoms have returned was a young lady, aged 25 years, who had only a mild peritoneal endometriosis without disease of the ovaries or uterus; surgery was limited to shortening of the ligaments. These four cases represent

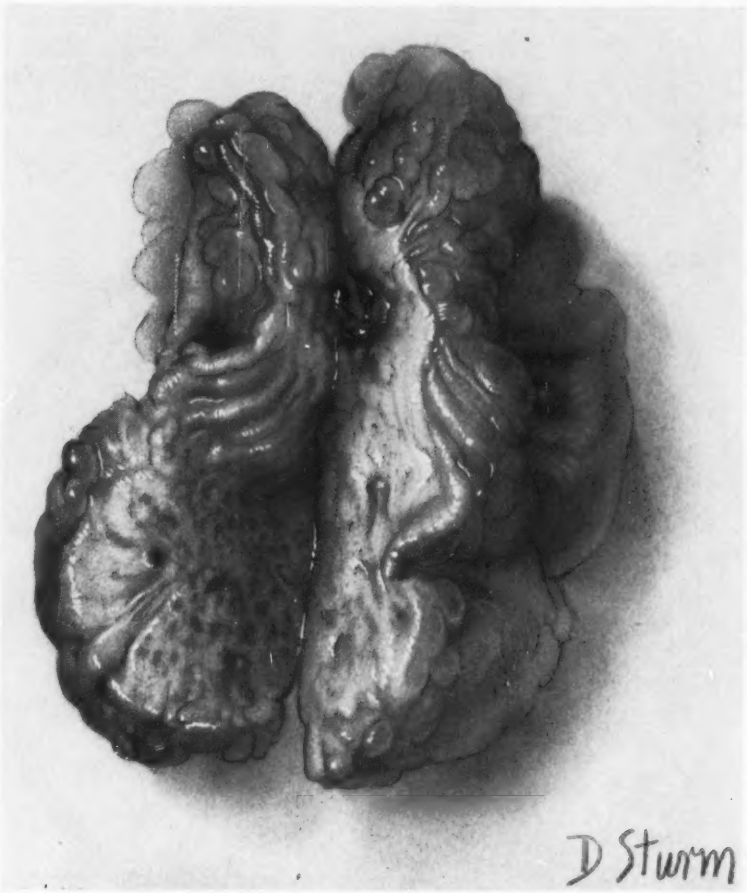

Fig. 1*B*.—Specimen open, showing interior.

22 per cent of the 19 patients whose ovarian function was not completely destroyed. Since the 4 patients from whom we have not heard had bilateral oophorectomies, this is probably a fairly accurate estimate of the results in the entire group. At the last report, none of the patients who had the more conservative operations had borne children.

TABLE IV

RESULTS OF OPERATION IN 120 CASES OF ENDOMETRIOSIS

		NUMBER PER CENT
Mortality	0	
Complete relief	112	93.3
Partial relief	3	2.5
No relief	1	0.9
No report	4	3.3

A large number of these patients have received theelin for control of menopausal symptoms. We were at first uncertain as to the effect of the drug and feared that it might possibly promote a recurrence or continuance of the endometrial process. Accordingly, we have examined a number of patients with this in mind. We have found no evidence that theelin reactivates the disease, nor does it appear to have any influence on the recession of growths left in the pelvis. We believe, therefore, that theelin should be given as a replacement therapy to make these patients comfortable.

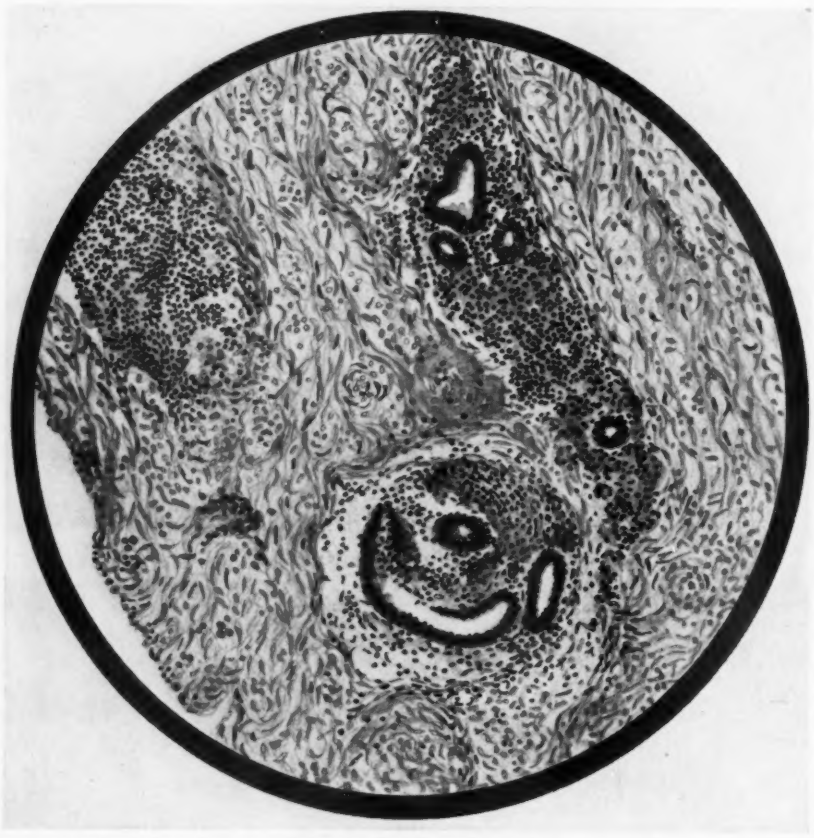

Fig. 1C.—Microscopic section of specimen, showing endometrial glands.

Four of the most unusual cases of this series are reported in detail. The first is that of a patient who had an endometrioma of the round ligament, from which menstrual blood passed through a small sinus opening into the groin.

CASE 1.—Mrs. J. R. S., a multipara, aged 41 years, came for examination because of a hernia which had been present for twelve years. Four months prior to her visit, she began passing blood and purulent material through the hernial mass at menstruation. This phenomenon was associated with severe pain, both local and referred down the thigh, but never with a rise of temperature.

On examination, a hard, nodular, inflammatory mass with a sinus opening was found in the groin and extending into the labium. The tissues over the mass were darker than normal. The cervix was in good condition, and the uterus was of normal size and movable, but retroverted. No mass could be found in the pelvis. The tentative diagnosis was endometriosis, with possibly incarceration of the tube in the hernial sac.

At operation, a firm tumor, approximately 2 by 3 inches in diameter, was discovered in the region of the groin and labium over the inguinal canal. From the outer side of the tumor, passing into the groin, was a sinus through which the patient had been menstruating. The mass was fastened deep in the fascia, making its liberation difficult. When freed from the labium and groin tissues, a hernial sac was discovered leading out from the inguinal ring. None of the intestine or omen-

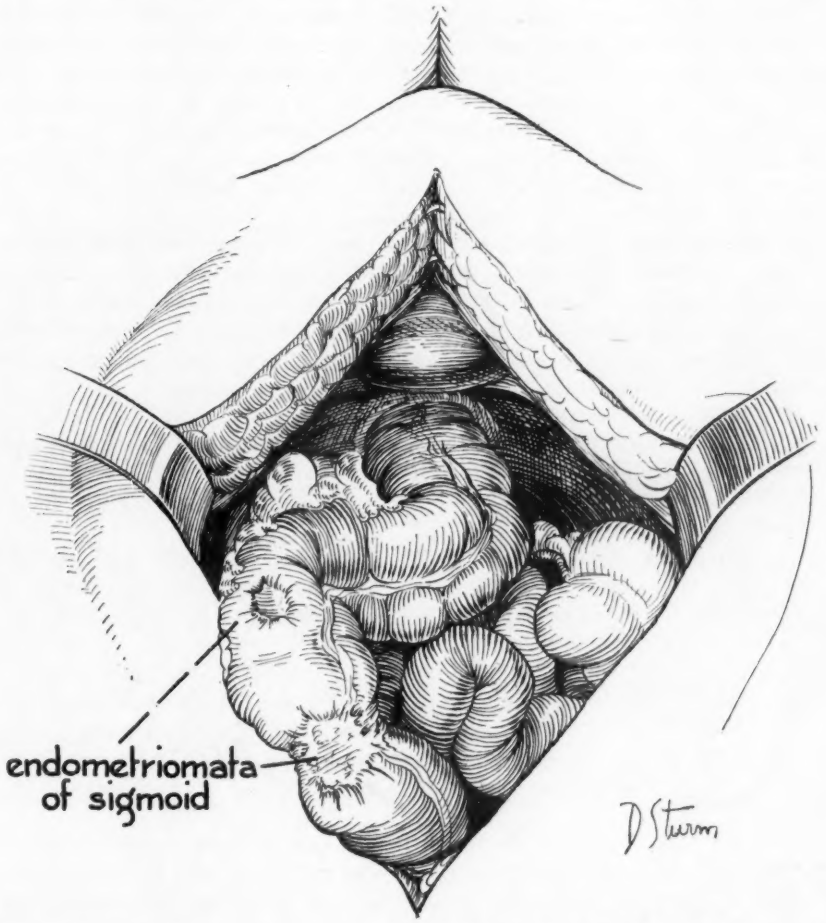

Fig. 2.—Two distinct endometriomas of the sigmoid of which the larger, distal lesion produced considerable obstruction. The intervening 2 inches of colon was entirely normal. The sigmoid was resected on clinical diagnosis of carcinoma; microscopic sections proved the lesions to be endometriomas. Mikulicz operation done and recovery followed.

tum was contained in the sac. The round ligament, which came out beneath the sac, was quite large and the tumor was attached to its extreme end over the pubic region.

The involved portion of the ligament was removed with the tumor, the remaining portion being fixed to the fascia to support the uterus. The hernial sac which had

led into the tumor was divided, transfixed and ligated, and the stump was Kocherized. Finger exploration of the pelvis through the opening revealed no indication of any other disease process. The hernia was repaired and the abdomen closed. The pathologic diagnosis of the tumor mass was inguinal endometrioma involving the round ligament.

The patient has had no further difficulty since her dismissal from the hospital, four years ago.

The patient in the following case had two endometriomas of the sigmoid, but no other evidence of the disease. The sigmoid was resected in the belief that the condition was malignant. This operation was performed ten years ago.

CASE 2.—Mrs. J. L. L., nullipara, was first seen in March, 1931, at the age of 39 years. She complained of intestinal disturbance, and stated that at each menstrual period her symptoms became more severe and were accompanied by the passage of blood and mucus from the bowel. All the details of the examination at that time are not now available; our record, however, shows that a mass was palpated in the cul-de-sac. Since I had not previously encountered a case of endometrioma of the sigmoid, the exploration was carried out under a diagnosis of cancer or diverticulitis.

When the abdomen was opened, a firm, nodular, contracting lesion was discovered in the mid-portion of the sigmoid, and a second, similar lesion one inch distally. In view of the finding of two distinct masses, it was believed that they were diverticula and were undergoing malignant change. There was no evidence of metastases in the glands or other organs. The uterus, tubes, and ovaries were practically normal and were not disturbed.

A three-stage resection was done. At the second stage, when the sigmoid was removed, a search was made for endometrial implants in the rectovaginal septum and elsewhere in the pelvis, though none were found. On microscopic section of the growths, a diagnosis of adenomyomas of the endometrial implant type was reported. The mucosa was not involved.

The patient was next seen in May, 1936, when she returned for a general checkup. She had had no menstrual pain nor any digestive symptoms since the operation, five years earlier. The function of the colon had remained good, and she felt entirely well. No further masses could be detected in the pelvis.

Eighteen months later, in October, 1937, she consulted us again because of fatigue and pelvic discomfort. She was then 46 years old and was menstruating only at intervals of six months. Pelvic examination disclosed a tender, firm area in the cul-de-sac, which was regarded as an endometrioma. The uterus was of normal size. Since the patient was passing through the menopause, surgery was considered unnecessary.

At her last examination, in December, 1940, the patient's symptoms had subsided and menstruation had entirely ceased. The mass could still be palpated in the cul-de-sac, though it had diminished in size since the preceding examination.

The following case is also one of endometriosis of the sigmoid without involvment of other structures. Profiting by my experience in the previous case, I removed the ovaries and uterus, but left the sigmoid intact.

CASE 3.—Mrs. W. D. M., multipara, aged 36 years, consulted us in July, 1940. She was referred for treatment of a recurrent Bartholin cyst which had first appeared nine years earlier. In addition to this complaint, she gave a history of increasing dysmenorrhea, pelvic soreness, and metrorrhagia over a period of three years.

Aside from the pelvis, the examination revealed nothing abnormal. The uterus was of normal size, in good position, and movable. There was a large, tender Bartholin cyst, and the cervix was moderately lacerated, cystic, and eroded. In the cul-de-sac, a tender mass the size of an English walnut could be palpated, and in the left uterosacral ligament there was a thickened, tender area. The diagnosis was pelvic endometriosis.

The cyst was incised and drained, and when healing was complete, operation for the pelvic condition was carried out.

The cervix was coned and the cystic sac excised. When the abdomen was opened, the uterus, ovaries, and tubes were found to be normal. The large, tender area previously detected proved to be an indurated napkin-ring tumor of the sigmoid, with fixation to the uterosacral ligament and posterior uterocervical juncture. The entire circumference of the sigmoid was puckered into a fold and the growth presented every appearance of cancer. A thorough search revealed no endometrial implants on any of the pelvic structures. A few inches higher on the sigmoid, however, there was another small puckered area. This was excised, and a diagnosis of endometrioma was reported on frozen section. It was then believed that the larger tumor was also an endometrioma. Accordingly, the uterus, tubes, and ovaries were removed, the sigmoid dropped back into its normal position, and the abdomen closed. Recovery followed without incident.

On request, the patient returned six weeks postoperatively for a check-up and roentgenographic examination of the colon. The pelvis was in good condition and she had no complaint other than the usual menopausal symptoms. The bowel function was normal. Proctoscopic examination was negative. A roentgenogram revealed some spasticity of the sigmoid, but no evidence of an encircling lesion.

When last heard from, in January, 1941, five months after operation, the patient stated that she was still taking theelin, but otherwise felt like a new person.

The last case is one of multiple endometrioma of the omentum associated with red degeneration of the uterus. I had never before or have never since observed a combination of these two conditions.

CASE 4.—Mrs. J. H. H., aged 46 years, nullipara, came for examination in January, 1938, because of pain in the lower abdomen and down the thighs. The pain had begun one week earlier, had been sufficiently severe to keep her in bed, and had been accompanied by a rise of temperature. She had also lost several pounds in weight since the onset of the pain. Until two months previously, her menstrual periods had always been regular; since that time, she had menstruated more often and more freely than usual.

Palpation of the abdomen revealed a large pelvic mass, irregular in outline, and extending almost to the umbilicus. On pelvic examination, the mass was found to be firm and partially fixed. The cervix was normal. The preoperative diagnosis was fibroid tumor.

Exploration revealed two large fibroids posteriorly and several smaller tumors on the anterior wall of the uterus. There was a considerable amount of red discoloration of the serous covering of the uterus, and the surrounding tissues were waterlogged and inflammatory. When the uterus was removed and opened, an area of red degeneration approximately 4 inches in diameter was found in the center of the largest fibroid. This accounted for the edema and inflammatory reaction of the tissues and explained the patient's fever. Both ovaries contained simple cysts and were removed with the tubes, the latter being normal.

There were no endometrial implants on the pelvic structures. In the omentum, however, which was thicker than normal, were two firm areas, not unlike metastasizing carcinoma. Both were excised and were reported by the pathologist to be endometriomas.

The patient's postoperative course was smooth and she has since been entirely well.

The last two of the foregoing cases are striking examples of the misleading symptoms, and even lack of symptoms often presented by endometriosis, and the difficulty of making a diagnosis from clinical evidence. Admittedly, such cases are rare, yet they show that unless one is mindful of the possibilities and makes a thorough search of all the organs, an error in treatment or inadequate treatment is not unlikely. This is no less true when the disease process clearly involves the pelvic structures.

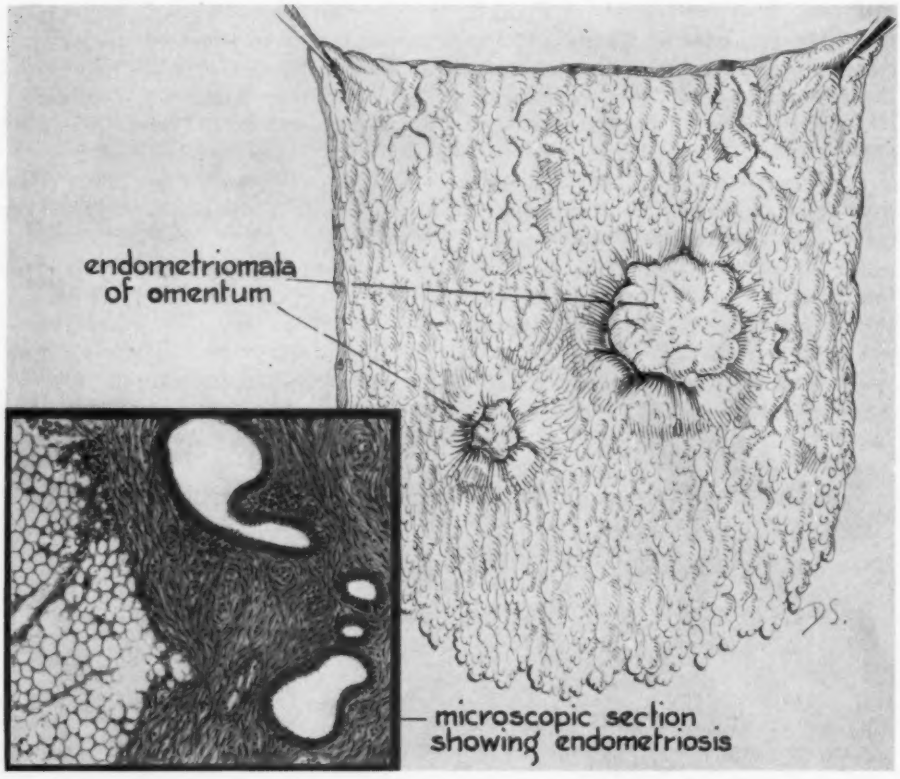

Fig. 3.—Two endometrial tumors of the omentum. No others were found in the abdomen or pelvis. Insert shows microscopic picture of endometrial tissue found in one of the tumors.

One needs merely to review the reported incidence of endometriosis as diagnosed in our hospitals, as compared to the incidence in private clinic practice, to appreciate the fact that it is recognized in only a small proportion of cases. Fallas and Rosenblum[4] report an incidence of 1.62 per cent in pelvic laparotomies in two private hospitals in Los Angeles. This figure is probably low for private hospitals. Perhaps the percentages found in two of the largest private institutions in Memphis are more typical. The records from which they were taken cover only a short period, nevertheless, they are sufficient to illustrate our point.

In the Methodist Hospital, during 1938, 1939, and five months of 1940, a diagnosis of endometriosis was made in 38 of 1170 pelvic operations, or 3.8 per cent. A complete report could be obtained from the Baptist Memorial Hospital only for the year 1939: endometriosis was recognized in 27, or 4.7 per cent of 576 cases in which the pelvic cavity was opened. Also of interest is the fact that at the John Gaston Hospital, which is a teaching institution devoted almost entirely to charity patients, a diagnosis of endometriosis was made in 12 of a total of 929 pelvic laparotomies performed during 1939 and 1940, representing an incidence of 1.3 per cent. In similar reviews, Long and Strecker[6] found a diagnosis of endometriosis in 0.96 per cent of pelvic laparotomies at the St. Anthony Hospital, a charity institution in Oklahoma City, and Pumphrey[8] encountered an incidence of 2.23 per cent in pelvic operations at the Miami Valley Hospital, also a general hospital, in Dayton, Ohio.

Compared with Meigs'[7] reported incidence of 32.2 per cent of cases of endometriosis in abdominal gynecologic operations in private practice, and even with my finding of endometriosis in 17 per cent of pelvic laparotomies, these figures speak for themselves. Certainly, they call in forceful terms for a better understanding and a wider recognition of this disease.

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ELEVATION OF THE FIRST METATARSAL BONE WITH HALLUX EQUINUS

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AN INTERESTING deformity of the great toe and first metatarsal bone has been observed for a number of years at the University Hospital. There is no doubt that this condition has been recognized by many observers but specific reference to it is rare in the available literature. Lapidus has recently described this deformity and has presented his conception of the etiologic factors, which are further substantiated by this report, and an operative procedure for its correction.

The purpose of this communication is to offer an explanation of the productive mechanism and to present methods of prevention and correction based upon forty-two examples of this deformity in thirty-eight patients.

CLINICAL FEATURES

In general, one might describe the deformity as a dorsal flexion deformity of the first metatarsal and a plantar flexion deformity of the great toe. It commonly results from a muscular imbalance of the foot.

In the early stage the deformity is not fixed. Passively the first metatarsal assumes its normal position and the great toe can be dorsiflexed normally. Because the deformity is on the basis of muscular imbalance, the incipent stage is mainly apparent when the patient is weight-bearing and particularly when he is walking. If the inequality of the muscle pull is not marked the deformity may never advance beyond this stage. However, in many cases the causative factors are sufficient to produce a fixed deformity with the subsequent development of pain over the dorsal aspects of the first metatarsal head where a bunion may develop. Even in advanced cases the abnormality is always more marked with active use of the foot in weight-bearing.

The Great Toe.—Usually the entire toe is in a position of flexion at the metatarsophalangeal joint. Less commonly the proximal phalanx has a flexed attitude but the distal phalanx is hyperextended. Hallux valgus may be associated.

The First Metatarsal Bone.—In the weight-bearing position the head of the first metatarsal is seen to be displaced upward so that the longitudinal axis of the metatarsal shaft may be horizontal or even directed anteriorly and slightly upward. The first cuneiform bone may also be tilted upward. A small exostosis may form on the dorsal surface of the head of the metatarsal.

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The First Metatarsophalangeal Joint. The metatarsophalangeal joint may present a subluxation if the flexed position of the phalanx is sufficient. If the deformity exists for some time, secondary degenerative changes may occur over the dorsal nonfunctioning portion of the articular surface of the metatarsal.

Soft Tissue Changes.—If the deformity becomes fixed the metatarsophalangeal joint presents a true flexion deformity of varying degree with the metatarsal more or less fixed in a dorsal flexed position at the metatarsocuneiform joint or at the first cuneoscaphoid joint or both. Contractures of the capsules of these joints may occur. It is not uncommon to have a true shortening of the flexor hallucis brevis muscle. A callosity often forms at the abnormal point of weight-bearing on the great toe and a callus and bursa may be present over the dorsal prominence of the metatarsal head.

Various primary diseases are associated with this deformity. However, the mechanisms of production of the deformity are, in the main, two in number. The first, and most frequent, is a muscular imbalance acting upon the first metatarsal causing this bone to assume a dorsiflexed position. The plantar flexed attitude of the hallux is secondary. The second mechanism is a muscular imbalance causing a plantar flexed position of the great toe, with secondary upward displacement of the first metatarsal.

GENERAL PRODUCTIVE MECHANISMS

I. *Primary Dorsiflexion Deformity of the First Metatarsal With Secondary Plantar Flexion Deformity of Hallux, Thirty-Six Examples.*

The upward displacement of the first metatarsal is due to a strong dorsiflexor muscle in the presence of a weak or absent plantar flexor muscle of this bone. Normally, the anterior tibial muscle by virtue of its insertion, raises the first cuneiform and base of the first metatarsal bone and thus can be considered a dorsal flexor of these two bones. The peroneus longus muscle opposes this action by exerting a plantar flexing force upon the base of the first matatarsal. Upward displacement of the first metatarsal can be produced by a strong anterior tibial muscle, or its substitute, in the presence of a weak or absent peroneus longus muscle. With the first metatarsal displaced upward the great toe is actively flexed to establish a point of weight-bearing for the medial portion of the forefoot and to augment the push-off in walking. Weakness of the dorsiflexor muscles of the hallux favor, but are not necessary for, the development of this position of the toe.

II. *Primary Plantar Flexion Deformity of the Hallux With Secondary Dorsiflexion Deformity of the First Metatarsal, Six Examples.*

Primary plantar flexion deformity occurs in the foot which is paralyzed except for an Achilles group of variable strength and strong flexors of the toes. The patient utilizes the flexor muscles of the toes

to help steady the foot upon the leg in weight-bearing and to supplement the push-off in walking. The great toe and its flexor muscles assume a large share of this added function and the hallux may be more or less constantly held in plantar flexion with active use of the foot. It is necessary for the head of the metatarsal to displace upward to accommodate for this weight-bearing position of the great toe.

In all cases of plantar flexion deformity of the great toe in type I or II, a strong flexor hallucis brevis muscle was a factor in the production of this deformity.

CLASSIFICATION OF CASES ACCORDING TO UNDERLYING DISEASE

Specific Productive Mechanisms

I. *Anterior Poliomyelitis, Twenty-Seven Examples.*—The primary dorsiflexion deformity of the first metatarsal may be the result of muscular imbalance due to the disease (2 examples) or muscular imbalance created by tendon transference (19 examples). Primary plantar flexion deformity of the hallux occurred only as a result of this disease in our series of cases (6 examples).

A. *Weak or completely paralyzed anterior tibial muscle, strong peroneal muscles; transference of peroneus longus muscle alone or peroneus longus and brevis muscles to the region of insertion of the anterior tibial muscle, thirteen examples* (Table I, Cases 1 to 13 inclusive): Each case had a valgus deformity of the foot. Four patients exhibited a plantar flexion deformity of the first metatarsal bone before operation. The foot was stabilized by triple arthrodesis in all cases except two. The peroneus longus tendon was transferred generally by way of the anterior tibial tendon sheath to a new insertion in the base of the first metatarsal (10 cases), or to the first cuneiform bone (3 cases). If the peroneus brevis tendon was also transferred it was inserted into the base of the second metatarsal (1 case) or into the first or second cuneiform bone (4 cases). From one to six years after the tendon transference, the primary dorsiflexion deformity of the first metatarsal became evident (Fig. 1). The secondary plantar flexion deformity of the hallux appeared concomitantly. The flexor hallucis brevis muscle was very strong in each case except one. Possibly because of this fact, this patient did not develop a plantar flexion deformity of the great toe which maintained a normal relationship with the first metatarsal head, thus not touching the ground in the weight-bearing position (Table I, Case 2).

In this group the primary cause of the deformity is the reversal of action of the peroneus longus muscle upon the first metatarsal brought about by the tendon transference. It is noteworthy that the four patients with plantar flexion deformity of the first metatarsal preoperatively developed a dorsiflexion deformity of this bone after operation. To establish a medial weight-bearing point for the forefoot, the flexor hallucis brevis muscle maintains the great toe in sufficient plantar

flexion and thus is a definite contributing factor. The transferred peroneus longus muscle maintained practically normal strength, which is, of course, a prerequisite to the development of the first metatarsal displacement. In exactly similar cases except for weakness of the peroneus longus tendon after transference, the deformity did not develop. The triple arthrodesis is apparently not a factor in the development of the deformity inasmuch as two patients did not have this operation and a third presented the deformity before stabilization was done.

B. *Gastrocnemius and soleus muscles completely paralyzed or very weak. Anterior tibial muscle normal strength, eight examples:*

(a) *Peroneal muscles completely paralyzed, two examples* (Table I, Cases 14 and 15).—Each case presented a calcaneocavovarus deformity. A triple arthrodesis was done in one and a triple arthrodesis plus

Fig. 1 (Table I, Case 5).—*A*, Lateral roentgenogram of foot 16 months after a Dunn triple arthrodesis and transference of peroneus longus and brevis into first cuneiform for paralytic pes valgus. The first metatarsal-great toe deformity is minimal.

B, Lateral roentgenogram of foot showing well-developed elevation of first metatarsal with hallux equinus.

C, Photograph of foot showing the deformity; note the skin irritation over the dorsal aspect of the first metatarsal head.

D, Photograph of foot 6 months following operative correction of first metatarsal-great toe deformity.

transference of the tibialis posticus, the flexor hallucis longus, and the flexor digitorum longus tendons to the calcaneus was carried out in the other (Fig. 2).

The cause of the dorsiflexion deformity of the first metatarsal is the strong anterior tibial muscle unopposed by a functioning peroneus longus muscle. The strong flexor hallucis brevis muscle is a secondary factor.

TABLE

EVALUATION OF MUSCLE POWER IN CASES

NO.	PATIENT	FOOT DEFORMITY RESULTING FROM PARALYSIS	G.S.†	P.T.	A.T.	P.L.	P.B.	P.TER.	F.H.L.	F.H.B.
1	R. S.	Planovalgus	1	0	0	1	1		3	1
2	D. D.	Valgus	N	2	0	N	N		N	N
3	L. W.	Valgus	N	0	0	N	N	1	0	N
4	C. B.	Valgus	N	2	0	N	0		1	N
5	A. V.	Equinovalgus	N	0	0	1	1		0	N
6	N. D.	Valgus	1	0	0	N	1		3	N
7	R. H.	Valgus	N	N	0	N	N	N	N	N
8	E. R.	Equinovalgus	N	2	0	N	N		3	N
9	M. H.	Valgus	N	0	0	N	N		N	N
10	W. H.	Calcaneovalgus	3	0	0	N	N		N	N
11	R. S.	Valgus	N	1	0	N	N		3	4
12	E. P.	Valgus	1	1	0	N	2		3	N
13	R. S.	Equinovalgus	1	5	0	N	N		3	1
14	J. V.	Calcaneocavovarus	5	0	N	0	0		0	N
15	M. L.	Calcaneocavovarus	0	2	N	0	0		3	N
16	D. P.	Calcaneocavus	0	1	N	N	N		0	1
17	R. G.	Calcaneocavus	4	N	N	N	N		2	1
18	J. W.	Calcaneocavus	0	1	N	N	N		1	1
19	J. B.	Calcaneocavovarus	3	1	N	1	1		N	
20	J. R.	Calcaneus	5	N	N	N	N		N	N
21	E. P.	Calcaneovalgus	4	1	N	N	N		N	N
22	P. S.	Equinovarus	1	3	5	0	0		0	N
23	W. B.	Equinovarus	N	0	0	0	0		0	N
24	G. D.	Equinovarus	0	0	0	0	0		0	N
25	J. B.		0	0	0	0	0		0	N
26	J. B.		0	0	0	0	0		0	1
27	O. S.	Varus	2	0	0	0	0		0	N

*Explanation of muscle rating:

N—Normal

1—Very good; a muscle that can overcome gravity and moderate resistance but cannot perform the normal test

2—Good; a muscle that can overcome gravity and slight resistance only

3—Fair; a muscle that can overcome gravity but not resistance

4—Poor; a muscle that can carry out its action only when gravity is eliminated

5—Trace; a muscle that can be felt to contract but cannot move the part

0—Gone; a muscle in which no contraction can be felt.

†Abbreviation for muscles:

G.S.—Gastrocnemius-soleus

P.T.—Posterior tibial

I

DUE TO ANTERIOR POLIOMYELITIS*

E.H.L.	E.H.B.	F.D.L.	F.D.B.	E.D.L.	E.D.B.	OPERATIVE PROCEDURES PRIOR TO ELEVATION OF METATARSAL WITH HALLUX EQUINUS
2		1	N	3		Triple arthrodesis; *P.L. transfer to base of first metatarsal;* P.B. transfer to second cuneiform
2	2	1		2		Triple arthrodesis; *P.L. and P.B. transfer to first cuneiform*
N	2	0	N	2	3	*P.L. transfer to base of first metatarsal;* triple arthrodesis; P.B. transfer to second cuneiform
1	2	2		2		*P.L. transfer to base of first metatarsal;* triple arthrodesis
0		2		0		Vulpius operation; triple arthrodesis; *P.L. and P.B. transfer to first cuneiform*
3	2	3	N	3	N	Vulpius operation; triple arthrodesis; *P.L. transfer to base of first metatarsal*
3	N	N	N	N	3	Triple arthrodesis; *P.L. transfer to base of first metatarsal;* P.B. transfer to second cuneiform
3	N	2	N	4		Vulpius operation; triple arthrodesis; *P.L. transfer to base of first metatarsal;* P.B. transfer to second metatarsal
N	1	N		N		*P.L. transfer to base of first metatarsal*
N	N	2		1		Triple arthrodesis; *P.L. transfer to base of first metatarsal*
3		2		1		*P.L. transfer to base of first metatarsal;* triple arthrodesis
N						*P.L.* and E.H.L. *transfer to first cuneiform;* triple arthrodesis
3		1	1	0	0	Achilles tenotomy; *P.L. transfer to base of first metatarsal*
N		2	N	0		Triple arthrodesis
2		3		3		Triple arthrodesis; P.T., F.H.L., F.D.L. transfer to os calcis
2		N	N	N		Subastragalar arthrodesis; *P.L.*, P.B., and P.T. *transfer to os calcis*
1		N		2		*P.L.* and P.B. *transfer to os calcis*
2		2	2	2		Subastragalar arthrodesis; *P.L.*, P.B., and P.T. *transfer to os calcis*
1		N				Triple arthrodesis; *P.L.*, P.B., and P.T. *transfer to os calcis*
N	N	N	1	2	1	P.T., F.H.L., F.D.L., *P.L.*, P.B., *transfer to oscalcis,* triple arthrodesis
4	3	N				F.D.L., *P.L.*, P.B., F.H.L., and P.T. *transfer to os calcis;* triple arthrodesis
0	0	1	N	4		Achilles tenotomy; Panastragalar arthrodesis
0	0	0		0		Panastragalar arthrodesis
0	0	0	N	0		Panastragalar arthrodesis
0	0	0	N	0		No
0	0	0	1	0		No
0	0	0	0	0		No

A.T.—Anterior tibial
P.L.—Peroneus longus
P.B.—Peroneus brevis
P.Ter.—Peroneus tertius
F.H.L.—Flexor hallucis longus
F.H.B.—Flexor hallucis brevis
E.H.L.—Extensor hallucis longus
E.H.B.—Extensor hallucis brevis
F.D.L.—Flexor digitorum longus
F.D.B.—Flexor digitorum brevis
E.D.L.—Extensor digitorum longus
E.D.B.—Extensor digitorum brevis

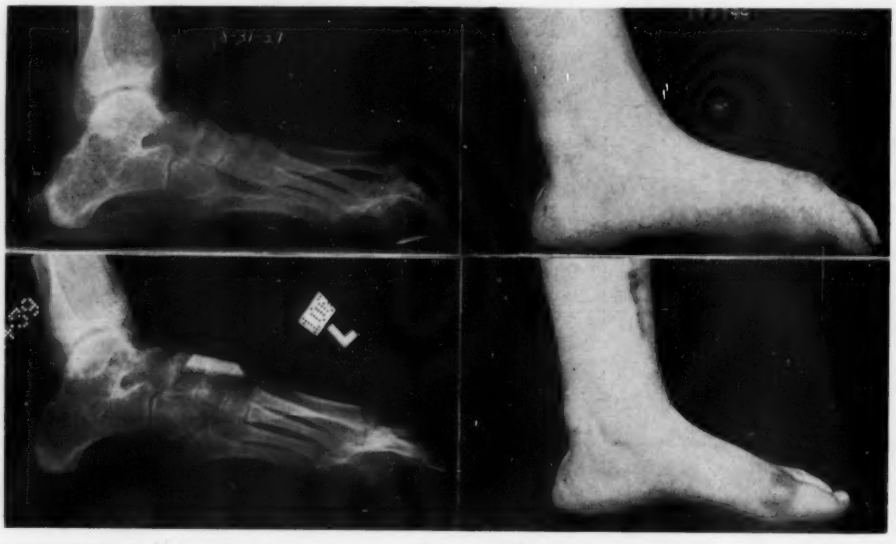
A. B. C. D.

Fig. 2 (Table I, Case 15).—*A*, Lateral roentgenogram of foot 6 months after triple arthrodesis for paralytic pes calcaneocavovarus.

B, Lateral roentgenogram of foot showing the elevation of the first metatarsal with hallux equinus.

C, Photograph of foot showing the deformity.

D, Lateral roentgenogram of foot 6 months after operative correction of first metatarsal-great toe deformity. (In this case the tibial graft was placed medially.)



A. B. C. D.

Fig. 3 (Table I, Case 16).—*A*, Lateral roentgenogram of foot 10 years after astragalocalcaneal arthrodesis and transference of peroneus longus, peroneus brevis, and posterior tibial tendons to calcaneus for paralytic pes calcaneocavus; the elevated first metatarsal with hallux equinus is well developed.

B, Photograph of foot as shown in *A*.

C, Lateral roentgenogram of foot 6 months after operative correction of first metatarsal-great toe deformity.

D, Photograph of foot 15 months after operative correction of first metatarsal deformity.

(b) *Peroneal muscles normal strength. Transference of peroneal tendons to os calcis, six examples* (Table I, Cases 16 to 21 inclusive).—Four cases had calcaneocavus deformities of the foot and one patient presented a pes calcaneocavovarus. A triple arthrodesis was done. Both peroneal tendons with or without other tendons were transferred to the os calcis in each case. The dorsal flexed position of the first metatarsal bone developed from two to twelve years after the tendon transference (Fig. 3).

Due to the transference of the peroneus longus the strong anterior tibial muscle causes dorsiflexion of the first metatarsal. The development of this deformity before the triple arthrodesis in 2 patients of this group again demonstrates that the stabilization is not a necessary factor. A strong flexor hallucis brevis muscle is contributive.

C. *Strong flexor hallucis brevis muscle. Gastrocnemius-soleus muscles strong, moderately weak, or paralyzed. Otherwise lower extremity essentially flail, six examples* (Table I, Cases 22 to 27 inclusive): The extremities were supported by braces. The flexor digitorum brevis muscle was also generally active. The gastrocnemius-soleus muscle group was completely paralyzed in three of the extremities while it was moderately weak in one and had normal strength in two. One patient had a strong flexor hallucis longus. To correct deformity and to stabilize the foot a panastragalar arthrodesis was done in three patients. To correct the metatarsal displacement the flexor hallucis longus in the one patient was sectioned without result (Fig. 4).

A. *B.*

Fig. 4 (Table I, Case 27).—*A*, Lateral roentgenogram of foot 3 years after panastragalar arthrodesis for paralytic pes equinovarus; the first metatarsal-great toe deformity is well developed.

B, Lateral roentgenogram of foot 2 months after operative correction of first metatarsal-great toe deformity. (The tibial graft was placed medially in this case.)

The strong flexor hallucis brevis muscle is the primary cause of the deformity, producing a plantar flexion deformity of the great toe. This muscle supplements the Achilles group of muscles in walking or when the action of the latter is absent, acts as a plantar flexor to gain some power of push-off in walking. In the standing position the muscle is

again very active as an aid in balance. The first metatarsal bone, of necessity, dorsiflexes when the hallux assumes this position.

II. *Congenital Talipes Equinovarus, Seven Examples.*—A primary dorsal flexion deformity of the first metatarsal bone and secondary plantar flexion deformity of the great toe may develop.

A. *Deformity well corrected. Persistent imbalance of peroneal muscles and tibial muscles, one example:* This patient was first seen because of a mild recurrence of equinovarus deformity. Tibial muscles possessed normal strength but the peroneal muscles were very weak. A triple arthrodesis was done and resulted in good correction. Six months later, on standing and walking only, the first metatarsal bone was dorsiflexed and the hallux plantar flexed. With the foot at rest there was no evidence of this deformity.

Fig. 4 *C.*—Photograph showing the deformity as in Fig. 4 *A*.

B. *Residual severe deformity consisting of equinus of the hind foot and dorsiflexion of the forefoot (Rocker feet), six examples:* The patients varied in age from 6 months to 5 years when treatment was started. All presented severe talipes equinovarus which either responded to conservative treatment and then recurred or failed to respond from the start to this form of therapy. In two cases there were long periods when the patients were not seen. Corrective soft tissue operations followed by either the Hoke or Dunn type of triple arthrodesis were done in all cases. In performing the stabilization in one patient both peroneal tendons were sectioned for purposes of exposure and were sutured at the completion of the operation. The metatarsal deformity gradually developed before the stabilization in four feet and after the stabilization in two (Fig. 5).

The metatarsal and great toe deformity in this group is, again, due to the imbalance which exists between the peroneus longus and the anterior tibial muscles. In the uncorrected congenital talipes equino-

varus the peroneal muscles are weak and the tibial muscles are strong. After complete correction of the deformity this muscle imbalance may persist and account for a dorsiflexed first metatarsal bone and a plantarflexed great toe which may, at first, be present only upon use of the foot.

Faulty manipulative corrections of a congenital talipes equinovarus may, unfortunately, produce the so-called rocker foot by forcibly stretching the ligaments and capsules which support the plantar aspects of the mid-tarsal joints. The hind foot remains in equinus and inversion while the forefoot is dorsiflexed and sometimes abducted. The action of the peroneus longus muscle is further weakened by the mechanical

Fig. 5.—*A*, Lateral roentgenogram of foot 3 months after a Dunn triple arthrodesis for congenital talipes equinovarus.

B, Lateral roentgenogram of foot 6 years later, showing a markedly elevated first metatarsal with hallux equinus.

C, Photograph of foot showing the first metatarsal-great toe deformity with a marked dorsal bunion over the first metatarsal head.

D, Lateral roentgenogram of foot 5 years after operative correction of first metatarsal-great toe deformity.

interference imposed by such a deformity. The anterior tibial muscle, strong from the beginning, becomes more powerful with attempts of the patient to gain dorsiflexion of the entire foot. Thus, the first metatarsal bone is gradually pulled into more relative dorsiflexion than the rest of the forefoot. The great toe is plantarflexed by its two flexor muscles to provide a point of weight-bearing medially and to aid the push-off which is limited and weakened by the equinus of the heel.

III. *Osteomyelitis of Os Calcis, Three Examples.*—The osteomyelitis was due to pyogenic organisms in two cases and tuberculosis in one. The disease was quiescent in each case and the patients had been walking upon the foot for years. Either because of operative removal or

destruction or both there was considerable loss of substance and deformity of the calcaneus. Because of infection and operations all presented considerable scarring about the hind foot. The infection had involved the ankle joints in the three cases causing a bony ankylosis. The subastragalar joint was ankylosed by bone in one and by fibrous tissue in two cases. The anterior tibial muscle possessed normal strength. The peroneal muscles were caught in scar tissue in one case, were of questionable strength in one, and had good power in the third. The flexor hallucis longus muscle was moderately weak in two cases and had no apparent action in one. The flexor hallucis brevis muscle possessed normal power in all cases. The dorsal flexion of the first metatarsal bone and plantar flexion of the hallux gradually developed. This deformity varied in degree and was always most marked on weight-bearing and walking (Fig. 6).

A. *B.*

Fig. 6.—*A*, Lateral roentgenogram of foot showing the ankylosed ankle and the marked deformity of the os calcis due to chronic, inactive, pyogenic osteomyelitis; the elevated first metatarsal with hallux equinus is well advanced.

B, Lateral roentgenogram of foot 1 year after operative correction of first metatarsal-great toe deformity.

The possible causes of the deformity in these cases seem to be three in number. Due to the considerable scarring about the heel the peroneus longus muscle may have been somewhat adherent to the scar tissue as it definitely was in one patient. The peroneal muscles may be further weakened by working at a mechanical disadvantage due to the deformity of the hind foot. The third factor is the ankylosis of the ankle with consequent loss of push-off from the Achilles group. This leads to the development of the flexors of the great toe, particularly the flexor hallucis brevis muscle, as secondary propelling muscles. All of these factors may be operative in these cases to explain the great toe-first metatarsal deformity upon the basis of muscular imbalance.

IV. *Cavus Feet, Three Examples.*—Two patients with cavus feet developed a primary dorsiflexion deformity of the first metatarsal bone with secondary plantar flexion deformity of the great toe. The etiology of the pes cavus was obscure, although the second patient had a spina bifida occulta.

CASE 1.—The first patient had bilateral pes cavus of moderate degree associated with mild weakness of the peroneal muscles. The plantar fascia was contracted and

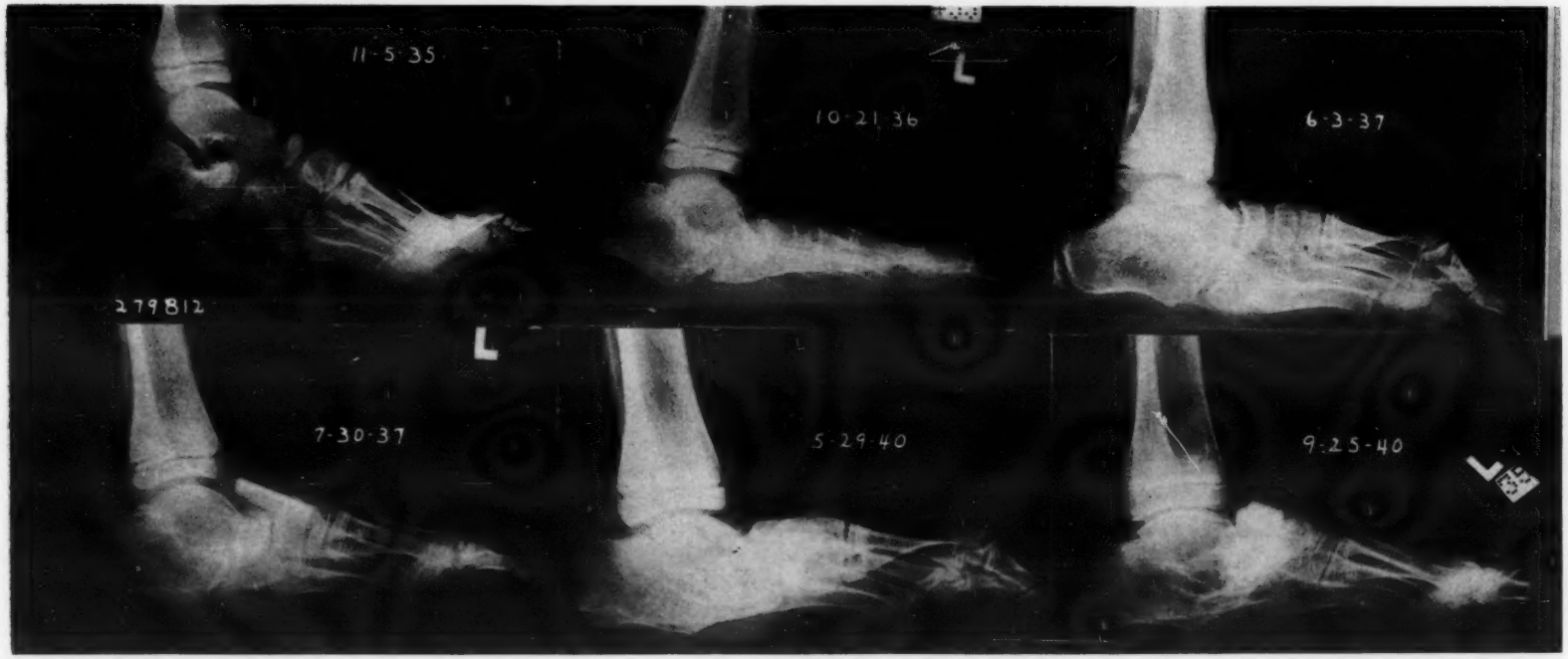


Fig. 7 (Case 1).—*A*, Lateral roentgenogram of foot 5 months after plantar stripping and transference of posterior tibial tendon to dorsum for pes cavus of moderate degree.

B, Lateral roentgenogram of foot 11 months later showing marked rocker foot deformity; a triple arthrodesis has been done but the marked pes planovalgus returned promptly.

C, Lateral roentgenogram of foot showing marked elevation of first metatarsal with hallux equinus; the mid-tarsal joint did not fuse.

D, Lateral roentgenogram of foot 6 weeks after operative correction of the first metatarsal-great toe deformity. The proximal end of the tibial graft has displaced out of its prepared bed.

E, Lateral roentgenogram of foot showing recurrence of the first metatarsal-great toe deformity because of the displaced tibial graft.

F, Lateral roentgenogram of foot 4 months after mid-tarsal osteotomy with bone grafts dorsally, correcting first metatarsal-great toe deformity.

overaction of the posterior tibial muscles was thought to be a contributing factor. Bilateral stripping of the plantar fascia and intrinsic muscles from the os calcis and transference of the posterior tibial tendons to the base of the third metatarsal bones were done. Within four months bilateral marked rocker foot resulted in a complete reversal of the original deformity. A triple arthrodesis of each foot failed to stabilize the foot in good position and the rocker feet continued. One year after the latter procedure, dorsal flexion deformities of both first metatarsals associated with plantar flexion deformities of the great toes were noted. Bunions were present over the dorsal aspects of the metatarsal heads (Fig. 7).

The reversal of the deformity from pes cavus to pes planovalgus in this case was due to the posterior tibial tendon transference to the dorsum of the foot. The dorsiflexed position of both first metatarsals with plantar flexion of the great toes was caused by the same muscular imbalance as in rocker feet complicating congenital talipes equinovarus.

CASE 2.—The second patient presented bilateral pes cavovarus associated with claw toes. The deformitiy was more marked in the left foot and the subsequent discussion refers to this foot. Pain over the plantar surface of the first metatarsal head was present and on weight-bearing he protected this joint by inverting the foot. No definite muscle weakness in the foot was apparent. The deformity was largely confined to the forefoot, the hind foot being essentially normal in appearance. The following operation was done upon the foot: arthrodesis of the first metatarsocuneiform joint with removal of wedges of bone from this joint to correct the downward displacement of the first metatarsal; transference of the tendon of the extensor hallucis longus to the neck of the first metatarsal; arthrodesis of the interphalangeal joint of the great toe; and dorsal capsulotomy of the first metatarsophalangeal joint to allow correction of the clawing of the great toe. Eighteen months later there was a dorsiflexion deformity of the first metatarsal with plantar flexion of the great toe. The patient continued to complain of pain in the first metatarsophalangeal joint.

The cause of the great toe-metatarsal deformity is not exactly clear. Although the tendon transference resulted in marked weakness of dorsiflexion of the great toe, the flexors of this toe also became weak. A very plausible explanation, but one which is not definitely proved by postoperative roentgenograms, is the possible interruption of or slowing of growth from the dorsal portion of the epiphyseal line of the first metatarsal bone caused by the wedge osteotomy of the metatarsocuneiform joint. The base of the wedge of bone removed from this joint was, of course, dorsal and trauma to the dorsal portion of the metatarsal epiphysis might have resulted. The persistent pain over the plantar surface of the first metatarsal head might also explain the deformity inasmuch as protection of this painful area would require overuse of the tibialis anticus muscle in order to lift the first metatarsal head from the weight-bearing surface.

V. *Pes Planovalgus, One Example.*—Following a twisting injury to the foot and ankle the patient developed a painful pronation of the right foot. There was considerable spasm of the peroneal muscles and of the long extensor muscles of the toes. Marked limitation of inversion and eversion of the foot was noted. The foot did not respond to conservative management and a triple arthrodesis was done. The deformity gradually recurred and a dorsal flexion deformity of the first metatarsal and plantar flexed great toe appeared. The stabilization had relieved the peroneal spasm. The tibialis anticus muscle was overactive during active use of the foot.

The metatarsal deformity apparently is primary and may be produced by essentially the same mechanism as in a rocker foot. The overactivity of the anterior tibial muscle to produce dorsiflexion and inversion in a pronated valgus foot overbalances the action of the peroneus longus upon the first metatarsal.

VI. *Paralytic Pes Planovalgus Associated With Recklinghausen's Neurofibromatosis, One Example.*—This patient presented a rather severe pes planovalgus which apparently resulted from involvement of the spinal cord by the neurofibromatosis. Definite paresis of the posterior tibial and gastrocnemius muscles was demonstrable. Conservative treatment failed and a triple arthrodesis was performed. The *peroneal tendons were sectioned in performing this procedure* because the operator reasoned that they were deforming factors. This was an error in judgment as subsequent events proved. The weakness of the plantar flexors of the foot was increased with a definite calcaneal type of foot developing. Eight months after operation a well-marked dorsal flexion deformity of the first metatarsal and plantar flexion attitude of the great toe was present.

The metatarsal deformity is primary and is due to the action of a strong anterior tibial muscle unopposed by a peroneus longus muscle. The flexor muscles of the great toe were utilized to enhance the pushoff mechanism in walking and also were used to plantarflex the great toe for a medial weight-bearing point. This case is comparable to the cases in Group B (a) caused by anterior poliomyelitis.

TREATMENT

Prophylaxis.—Nineteen cases of this deformity occurred as a result of tendon transference in anterior poliomyelitis. In these instances the balanced and opposing actions of the peroneus longus and anterior tibial muscles upon the first metatarsal had been underestimated before proceeding with tendon transference. Before transference of the peroneus longus tendon the effect of the loss of its normal action upon the first metatarsal should be carefully considered.

With paralysis of the anterior tibial muscle in a case adapted to tendon transference, the peroneus longus tendon or both peroneal tendons should be transferred to the region of the third metatarsal base or third cuneiform bone rather than to the region of insertion of the anterior tibial tendon. By this procedure the objectives of the tendon transference will be gained without resultant deformity of the first metatarsal bone. Another method that may be suggested is the transference of the peroneus brevis tendon to the anterior tibial tendon insertion, leaving the peroneus longus undisturbed. A triple arthrodesis is, of course, always indicated (Group I, A).

In cases of weak or paralyzed Achilles group of muscles with strong anterior tibial and peroneus longus muscles, the latter muscle should

not be transferred to the os calcis unless the anterior tibial tendon is transferred to the mid-foot (Group I, B,b).

Treatment of the Deformity.—If the muscle imbalance is not marked, the deformity may never become severe enough to warrant operative correction. In cases showing progressive deformity of the great toe and first metatarsal, operative correction is simplest when done early before the deformity has become fixed. Transference of the deforming muscle, either the anterior tibial or transferred peroneus longus, to the third metatarsal base may correct the dorsal flexion of the first metatarsal.

If the first metatarsal deformity has existed for some time, it becomes more or less fixed and more radical surgery is often indicated. The deforming tendon should be transferred to the mid-foot as already referred to and an arthrodesis of the joint or joints at which the dorsiflexion occurs should be performed, correcting the metatarsal displacement. This requires, as a rule, a corrective arthrodesis of the first metatarsocuneiform joint or the first cuneoscaphoid joint or both. This operation has given very satisfactory results in our experience (Table II). The dorsal aspect of the joint is opened by reflexion of the cap-

TABLE II

RESULTS OF OPERATIVE CORRECTION OF DEFORMITY

OPERATION	AVERAGE TIME POST-OPERATIVELY (IN MONTHS)	GOOD		FAIR		POOR		TOTAL NUMBER OF EACH OPERATION
		NO.	%	NO.	%	NO.	%	
Transference of deforming tendon	15	3	50	2	33	1	17	6
Corrective arthrodesis utilizing tibial graft dorsally	21	11	73	3	20	1	7	15
Transference of deforming tendon plus corrective arthrodesis utilizing tibial graft dorsally	3	1	100					1
Miscellaneous operations*	19	5	71	1	14	1	14	7
Summary		20	69	6	21	3	10	29

*Miscellaneous operations.

	RESULTS
1. Transverse osteotomy of proximal metatarsal shaft with dorsal tibial graft	Fair
2. Transverse mid-tarsal osteotomy with rotation of forefoot to correct first metatarsal displacement and removal of wedge of bone to correct adduction; transference of deforming tendon (transferred peroneus longus tendon)	Good
3. Corrective panastragalar arthrodesis to correct talipes calcaneocavovarus; section of deforming tendon (anterior tibial tendon)	Good
4. First cuneiform scaphoid fusion with reversal of plantar wedges of bone (talonavicular fusion); capsulotomy of first metatarsophalangeal joint to correct flexion deformity of hallux	Good
5. Triple arthrodesis, manipulation of forefoot into plantar flexion; tibial graft to defect in dorsal aspects of talonavicular joint	Good
6. First metatarsocuneiform arthrodesis; section flexor muscles of great toe; capsulotomy of first metatarsophalangeal joint to correct flexion deformity of hallux	Good
7. Transverse mid-tarsal osteotomy; manipulation of forefoot into plantar flexion; tibial graft to defect in dorsal aspect osteotomy line	Poor

sule and the cartilage is removed. With a thin osteotome a rectangular section of bone ¼ to ⅜ inch deep is removed from the dorsal aspects of the contiguous bones. These two sections of bone are cut into small pieces. The first metatarsal bone is manipulated into its normal position where it is held by an assistant. This replacement results in a wedge-shaped defect in the joint as the dorsal aspects of the contiguous bones swing apart. A bone graft of sufficient size to fill the rectangular defect and to bridge the dorsal gap in the joint is removed from the tibia and pounded into the prepared bed, maintaining the correct position of the metatarsal. Any space remaining in the joint is filled with small bone grafts. If arthrodesis of both the first metatarsocuneiform and first cuneoscaphoid joints seems advisable the technique is the

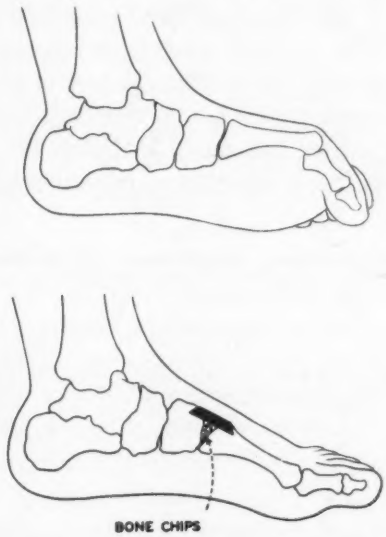


Fig. 8.—Drawings to illustrate the arthrodesis of the first metatarsocuneiform joint, utilizing a tibial bone graft and bone chips, to correct elevation of the first metatarsal with hallux equinus; the deforming muscle should be transferred to the mid-foot if the first metatarsal displacement is primary.

same, the tibial bone graft extending from the scaphoid bone across the first cuneiform into the base of the first metatarsal. If there is a fixed plantar flexion deformity of the great toe it usually responds to manipulation. In a small minority of cases a capsulotomy of the plantar aspect of the first metatarsophalangeal joint was also necessary. The foot is immobilized in a plaster cast with the corrected position of the first metatarsal well supported. Ankylosis is usually present in eight weeks (Fig. 8).

Other operative procedures have been used in correcting this deformity inasmuch as the treatment must be individualized for each case. Thus the correction of the first metatarsal deformity may be done at the mid-tarsal area as part of an osteotomy or triple arthrodesis which is necessary to correct other deformities and to stabilize the foot (Table II, Miscellaneous operations).

SUMMARY

Forty-two examples of elevation of the first metatarsal with hallux equinus have been reviewed. The modes of production and methods of prevention and operative correction of the deformity are presented.

The deformity is caused by a muscular imbalance of the foot which is the result of various primary diseases. An imbalance of muscles acting upon the first metatarsal caused the deformity in 86 per cent of the cases while 14 per cent were the results of muscular imbalance of the great toe.

The primary disease was anterior poliomyelitis in 64 per cent of the examples. Tendon transference accounted for the deformity in 70 per cent of the cases in this group (45 per cent of the total series). Before transference of the peroneus longus tendon careful consideration should be directed to the effect of such transference upon the first metatarsal. This tendon should not be transferred to the region of insertion of the anterior tibial tendon nor should it be transferred to the os calcis without regard for a strong anterior tibial muscle.

The results of operative correction of this deformity have been relatively good.

The author wishes to express his appreciation to Dr. C. E. Badgley, Dr. Martin Batts, and Dr. R. E. Mc Cotter for their help and advice in the preparation of this manuscript.

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A CASE OF LIVEDO RETICULARIS AND VASOSPASM TREATED BY SYMPATHECTOMY, WITH SOME NOTES ON SYMPATHETIC ANESTHESIA IN LABOR

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LIVEDO reticularis is a rather uncommon circulatory disorder of the skin which has been recognized for many years but the mechanism of which is poorly understood. It is characterized by a reticular bluish mottling of the skin which is intensified by cold and by dependency of the affected part. Closely allied to this condition is the so-called livedo racemosa in which there are raised or palpable cutaneous lesions in a distribution corresponding to the bluish areas in livedo reticularis. Also closely related is erythema ab igne, a condition in which a more or less permanent reddish or brownish discoloration of the same general pattern occurs as a result of exposure to heat.

The classification of livedo reticularis which Williams and Goodman[1] suggested is a very helpful one. These authors divided the cases into three groups. Cutis marmorata, the commonest form, occurs as a general rule rather diffusely over the body, is increased by cold and disappears when the body is warm, and is most frequent in infants, often disappearing as the child grows older. Livedo reticularis idiopathica is a more intense mottling which generally persists with variation in degree regardless of ordinary changes in the temperature of the skin. Livedo reticularis symptomatica is a similarly persistent mottling associated with some other disease which may affect the superficial vascular bed, such as the erythema induratum type of tuberculid,[2] syphilis,[3] or periarteritis nodosa.[4]

The case which I am reporting represents an unusual type of vasospastic disease in which livedo reticularis was present in the lower limbs. Because of the absence of pain with the uterine contractions of labor in this patient after she had undergone bilateral lumbar sympathectomy, I have been stimulated to investigate local anesthesia of the sympathetic nerves for the relief of pain in labor.

CASE REPORT

H. S., an 18-year-old white girl, came to the Johns Hopkins Hospital on May 29, 1940, complaining of bluish mottling of both lower extremities and of coldness and numbness of both feet. Her general health had been good. Two years previously, during the winter, a friend had called her attention to a bluish discoloration about both ankles. When first noticed it was evenly distributed in both legs and gradually spread in a symmetrical fashion down into the feet and farther up the legs.

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Recently it had been present in the lower half of both thighs. When she arose in the morning the mottling was slight and became more noticeable after she had been on her feet for a short while. She thought it was increased by exposure to cold; it was less prominent during the warm summer months but became even more extensive when cold weather returned. She said that the discoloration became less apparent when she warmed her legs before a fire or under bedclothes. During the winter in which the mottling was first observed she had also begun to complain of coldness of her feet and legs; she could not recall which came first. On slight exposure to cold the feet and legs would become extremely cold, and often there would be a mild aching tired feeling in the legs and feet and an annoying numbness of the feet and ankles. Emotional excitement did not seem to cause her feet to become cold. She thought that her feet and hands perspired more than normally. She had no edema or ulceration. Her hands were generally warm and became cold only on prolonged exposure to extreme cold. In recent months she had noted a very faint mottling on the dorsum of her left hand. It was of interest that the patient, as well as other members of her family, was accustomed to sitting with her feet on the rail of a stove when she came indoors on a cold day. No other members of the family had similar complaints. The family did not recall any mottling during her infancy.

When she was first seen in the outpatient department on a cool day but after she had been in a warm room for an hour or more, her lower extremities presented a striking appearance. There was a dirty blue reticular mottling beginning in the mid-thighs and covering the entire legs and feet. The central areas within the cyanotic rings were extremely pale and the appearance was much like that often seen in cadavers. The entire discolored area was very cold; the upper halves of the thighs were warm. The femoral arteries pulsated well. At times it was thought that a weak pulsation in the left posterior tibial artery could be distinguished, but this was not certain. No right posterior tibial and neither dorsal pedal pulsation could be felt. On elevation of the legs the pale areas increased in pallor and the mottled blue gradually became less prominent and eventually disappeared. The mottling was intensified when the limbs hung down. The hands were moderately warm and the radial pulses full, and there was no mottling of the upper extremities or trunk.

Two days later skin temperature studies were carried out. After the patient had been lying down in a warm room for some time the feet were slightly cool, the legs warm. The dorsal pedal pulsations were small but easily felt; the posterior tibial pulsations were full. There was a pinkish blue mottling up to the knees. On exposure to cold (room temperature 20° C.) the toes cooled to about room temperature, the temperature in the fingers dropped to 28° C., the mottling became more intense and extended up into the thighs, and the pinkish blue color gave way to a dusky blue. A very faint mottling appeared on the dorsum of the left hand. The dorsal pedal pulsations became almost imperceptible. When the body was warmed with blankets and heating pads, the exposed lower extremities gradually became warm, the pulses became stronger, and the mottling disappeared. After an hour and a quarter of body heating the temperature of the toes rose to 34° C.

She was admitted to the hospital on July 23, 1940; the mottling had been less prominent during the previous summer, but it was now very noticeable even during hot weather. Although it was a very hot day the feet were cool and the mottling was present. Fig. 1 is a photograph of a water color made on a hot day after brief exposure in a cold room. When vasospasm was more complete the mottling was even more extensive than is here represented. When there was moderate vasospasm a brilliant red reaction could be obtained over both the pale and the livid areas by pricking into the skin a solution of 1:1,000 histamine. No reaction occurred when 1 per cent mecholyl was pricked into the skin. These tests were not repeated when vasospasm was extreme.

The impression was that the patient had severe vasospasm and livedo reticularis of both lower extremities.

On July 25, the second, third, and fourth lumbar sympathetic ganglia on the right side, with the intervening chain, were excised through the usual extraperitoneal approach. After this operation no mottling was noted in the right lower extremity and it remained warm and dry, whereas mottling persisted in the left, and the left foot was usually cool and wet though covered by bedclothes. When the legs hung down, however, a faint pink mottling appeared in the right leg and foot. Even in a hot room (30.4° C.) the difference in temperature of the two lower extremities was striking: the toes were 6.5° warmer on the right side, the ankle 3° and the patellar region 2° C. The same operation was carried out on the left side on August 1, and she was discharged on August 7.

Her feet have remained warm and dry, there has been no discomfort or numbness, and she has had no discoloration except a faint pink mottling when her legs are dependent. She has gone through two winters without any difficulty. When her legs are dependent a faint mottling is present which is less extensive than it was before operation, the reticulations are much finer, and the color is an inconspicuous bright pink. The mottling disappears slowly when she lies down, a little more rapidly when her limbs are elevated; it gradually appears when the limbs are hanging down, a little more slowly when a venous tourniquet is placed about the thigh when the patient is recumbent.

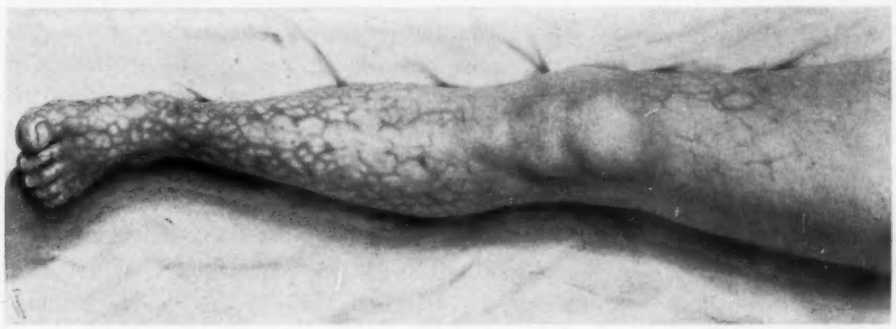

Fig. 1.—Photograph of a water color of the patient's right lower extremity.

The patient had her first child in August, 1941. When a show appeared she consulted her physician and was surprised to be told that she was having strong uterine contractions and was in active labor. She was admitted to a hospital, labor progressed rapidly, and she was delivered spontaneously of a normal infant. She said that she had no pain at all with uterine contractions up to the time of expulsion of the baby.

DISCUSSION

Kaposi,[5] who apparently first used the term livedo to designate localized and limited areas of cyanotic mottling in contradistinction to generalized cyanosis, felt that the mottling was due to distension of the veins. The superficial venous network does not, however, correspond to the pattern of livedo reticularis. Renaut[6] made studies of the arrangement of blood vessels in the skin by injections of Prussian blue, during which there first appeared rounded blue patches which he felt outlined the bases of vascular cones, each of which was fed by a deep artery at its apex and which represented areas of maximal circulation. As the injection was first being made these rounded areas were separated by

pale tracts which he thought were the peripheral portions of the vascular cones and represented areas of reduced circulation. As the injection proceeded, these areas also became blue. He thought that venous stasis might produce a dusky reticular network corresponding to the areas of reduced circulation. This explanation of the anatomic background of livedo was accepted by Adamson[7] and others. Lewis[8] was unable to repeat these observations with dye injections of the skin, nor was he able to substantiate them with observations of natural injections of the skin following release of pressure after an arm had been emptied of blood with an Esmarch bandage. Yet he concluded that the evidence pointed to a "correspondence between areas of mottling and main arteriolar territories, the maximal points of supply being in the center of the paler areas. This excess of blood flow, slight as it may be, would explain an associated increase of minute vessel tone and pallor. Given that the marginal areas are areas to which blood flow is slightly less, then they would be more susceptible to damage, and here the tone of the vessels, originally low, would tend to become more or less permanently inefficient, leading to quite distinct changes in responsiveness, changes that might even become associated with refractoriness." Although Lewis was unable ordinarily to detect anything but negligible and inconstant differences in temperature between the pale and the colored areas, as might be expected if the difference in flow is slight, he did find that the pale areas in a case of erythema ab igne were, on an average, 0.08° C. warmer than the dark areas, indicating, if anything, a slightly greater blood flow in the pale areas.[8, 9] Lewis stated that capillaries and venules are the same in number in the pale and the livid areas; Barker, Hines, and Craig[10] stated that capillaries are more numerous in the livid areas and usually more dilated and with slower blood flow.

From the data available it appears that the best explanation of the mechanism of livedo is as follows: There are areas of maximal blood supply in the skin, perhaps from capillary arborizations from central arterioles which enter the skin from below. In these central areas the tone of the capillaries is slightly greater and the blood flow slightly faster than in the surrounding periphery. Either through organic changes in the blood vessels or through vasospasm of the arteries and arterioles supplying the skin, the capillary atony and stagnation of blood flow in the peripheral areas is further increased. This increase brings about a livid discoloration in annular rings surrounding central pale areas. The discoloration is intensified by exposure to cold, which further increases the vasoconstriction of the arteries and arterioles supplying the skin. The livid areas disappear or change to a pink color with finer reticulation when vascular spasm is released by warming the body of the patient or by sympathetic interruption. Dependency of the affected part similarly brings about some intensification, possibly through the same mechanism, for though there is disagreement on this point[11, 12] it is maintained by some investigators that vasoconstriction occurs when the legs are in a dependent position.[13, 14] The persistence of some

mottling after body warming or sympathectomy, as in my case (although the discoloration is now pink and not blue) is due to the fact that in some instances the atony and dilatation of the capillaries may be more or less permanent. In order to explain the disappearance of the livedo on elevation of the affected limb it seems best to assume that the venules draining the capillary bed in the peripheral annular zones where there is reduced blood flow and capillary atony are likewise somewhat dilated. When the limb is dependent the increased venous pressure would exaggerate this dilatation and stagnation in the venules and would increase the livedo; when the limbs are elevated these venules would empty and diminish the mottling. This explanation would account for the changes in appearance with dependency and elevation of the limb after sympathectomy has been performed and any normal vasoconstrictor effects of dependency presumably have been eliminated.

It is interesting that Cavafy[15] in 1883 wrote: "I think the condition is probably due to a vasomotor neurosis, allied to the local asphyxia of Raynaud, but the share taken in its production by arteries and veins is not easy to apportion. In temporary mottling from cold we have probably to do with spasm of the terminal arterioles of the skin and consequent overfilling (from diminution of pressure *a tergo*) of capillaries and veins. . . ."

Barker, Hines, and Craig[10] have recently reported thirteen cases of livedo reticularis and have expressed the opinion that there are usually organic changes in the arterioles of the skin as well as chronic vasospasm. Several of their patients had ulcers of the legs and superficial gangrene of the toes. They performed lumbar sympathectomy in three cases. In two, in which there was gangrene of the toes, the feet became warm, the toes healed, no further gangrene developed, and the livedo almost completely disappeared. In the third, in which there was an ulcer of the leg and gangrene of several toes, the operation was followed by healing of the ulcer and toes but the ulcer reappeared after a year and amputation was eventually necessary. In this case the livedo persisted but the color of the livid areas was pink except on exposure to extreme cold.

The fact that my patient went through the first stage of labor without feeling any pain with uterine contractions was a very stimulating and somewhat surprising occurrence. The course of the afferent pain fibers from the uterus is not fully understood. Whether they pass from the superior hypogastric plexus directly into the lumbar sympathetic chains or whether all or part of them pass up through the aortic plexus to enter the sympathetic chains at a higher level, is not known. With regard to my patient one cannot be certain whether there was a causal relationship between the excision of the lumbar sympathetic chains and the absence of pain with uterine contractions. She certainly reacted normally to other painful stimuli.

I know of one other instance in which a patient on whom bilateral lumbar sympathectomy had been performed has recently gone through

parturition. Four and one-half years previously sympathectomy had been performed elsewhere for Raynaud's disease and scleroderma. The sweating defect would indicate that the operation undoubtedly included resection of both second and third lumbar ganglia. Though it is very difficult to interpret her subjective sensations during labor they merit consideration. At the time of delivery those attending her were not impressed with anything unusual but felt that her labor was very easy. On careful questioning she states that she was having no pain at all when her membranes ruptured spontaneously at 1:30 A.M. while she was lying in bed. She went to the hospital shortly afterward and fleeting uterine contractions were noted by the examiners. She slept soundly without medication until about 6 A.M. By 8 A.M. labor was definitely established. All during the morning she had no sensations with the uterine contractions except an ill-defined feeling within the abdomen of an intermittent tightening and relaxation, not painful, a sensation akin to that experienced when the skin is stretched and then released. In the afternoon she began to have an aching discomfort in the back which was constant and which was not, as well as she can recall, exacerbated during uterine contractions. The feeling of tightness became stronger. At 4:15 she experienced her first severe pain, an agonizing pain as if she were being squeezed. The exact localization is not recalled, but she thinks it was felt over the abdomen as well as in the pelvis. After three or four such pains she was taken to the delivery room and at 4:45 an 1,860 Gm. child was delivered under sodium pentothal anesthesia. It is not possible to say whether this relatively painless first stage was related to the sympathectomy or whether it was a coincidental easy premature labor.

It will be interesting to learn if other women who have undergone bilateral lumbar sympathectomy have any alteration of subjective feelings during labor or whether they have the customary pain. Regardless of whether the absence of pain in my patient was coincidental or the result of her previous sympathectomy, or whether the second patient had diminished pain as the result of her operation, the question of the relation between lumbar sympathetics and uterine pain deserves fuller study. Further study and observation of cases may or may not provide evidence to suggest that bilateral lumbar sympathectomy may be helpful in alleviating painful uterine conditions or that this operation may be advantageously combined with resection of the hypogastric plexus.

The case reported has led me to investigate the effect of sympathetic anesthesia in labor. A sufficient number of cases has been studied to permit me to say that an effectual injection of a local anesthetic solution into the region of the lumbar sympathetic nerves on both sides will alleviate temporarily the abdominal pain associated with uterine contractions apparently without interfering with the frequency or forcefulness of the contractions and without deleterious effect upon fetus or mother. A preliminary report of this study will be published shortly. As far as I know, direct bilateral injection of the lumbar sympathetic nerves has not been used for abolishing the pains of labor. Some years ago

Cleland,[16] believing that the afferent pain fibers from the uterus entered the spinal cord through the eleventh and twelfth spinal roots, injected these roots in five women in labor and obtained analgesia over the lower abdomen and cessation of pain with uterine contractions. Several years previously Dellepiane and Badino[17] had reported alleviation of pain with uterine contractions from a unilateral injection in the region of the third lumbar sympathetic ganglion.

Although lumbar sympathetic anesthesia may ultimately prove of aid in alleviating pain during the first stage of labor, it is my hope that it will not be adopted in general obstetric practice until numerous problems concerned with its use have been thoroughly investigated.

SUMMARY

An unusual case of vasospasm of the lower extremities associated with livedo reticularis is presented and the mechanism of livedo is discussed. Lumbar sympathectomy gave an excellent result and appears to be indicated in cases of this kind. Because of absence of pain with the uterine contractions of labor in this patient, the possibility of inhibiting painful stimuli from the uterus by interruption of the lumbar sympathetic impulses is being investigated.

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EMBOLECTOMY FOR RIDING EMBOLUS OF ABDOMINAL AORTA*

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PROBABLY the first attempt to remove an embolus by arteriotomy was made in 1895 by Ssabanjew,[1] a Russion surgeon, and although he was unsuccessful, post-mortem examination nineteen days after operation showed the suture line in the blood vessel to be free from clots. Following this attempt, several surgeons did arteriotomies but without success. Although also unsuccessful, Trendelenburg's[2] operation for pulmonary embolism performed in 1907 encouraged further attempts in this field. However, all attempts at embolectomy were unsuccessful until Labey's successful embolectomy of the femoral artery, as reported in 1911 by Mosny and Dumont.[3] In the following year, 1912, Alexis Carrell received the Nobel Prize from the King of Sweden for his researches on the suture of the blood vessels and the transplantation of vessels and organs. It was also in this year that Key[4] reported the second successful embolectomy of the femoral artery. The success of this case, the technique employed by Key, and the work of Carrell greatly stimulated the interest of surgeons in Sweden. By the end of 1927 Key[4] was able to collect 216 cases from the literature and hospital reports, 145 of the patients having been operated upon in Sweden. About five years later, Strombeck, Hindmarch, and Sondberg[5] of Stockholm collected 364 cases of embolism of the arteries of the extremities, all of the patients having been operated upon in Sweden. Since that time there has been an increasing number of reports from the Scandinavian countries and from this country.

In 1929 Burrow and Flint[6] reported an unsuccessful attempt to remove an embolism at the bifurcation of the abdominal aorta by operation. This case was of considerable interest in that the embolectomy was not performed until thirty-six hours after onset, at a time when there was marked evidence of peripheral circulatory impairment such as mottling, loss of pulsation, complete loss of function of the extremities. All of these symptoms disappeared after removal of the embolus through an incision in the terminal aorta, but the patient died twenty-six hours after operation, from cerebral hemorrhage with infarction, as revealed at necropsy. Several cases of embolectomy of the aorta were reported subsequently with the same result, the interval between operation and death varying from a few hours to a few days. In 1931 Mason and Warren[7]

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reported an embolectomy of the aorta with death from a renal infarction twenty-six hours after operation. Circulation was good in both legs after the operation until death.

For the most part, the results of embolectomy in the terminal aorta have been poor. In 1932 Pearse[8] made a critical survey of embolectomy of the extremities, including seven embolectomies of his own in six cases. This survey apparently included the 216 cases reported by Key in 1929. As reported by Pearse, there were 282 embolectomies including thirty-four cases of embolism of the abdominal aorta, 131 of the common femoral, and forty of the brachial artery. Pearse states that for an embolectomy to be considered successful, the patient must survive at least a month after the operation. Of Pearse's collected cases, 133, or 48 per cent of the patients, fulfilled this criterion, a fact which should encourage surgeons to continue their efforts.

Etiology in the patient in the case to be reported was essentially the same as it had been in practically all of the previously reported cases. That is, it has its origin as a thrombus which begins in the left heart and from that point is floated into the arterial tree; if it is small enough, of course, its drifting will come to an end beyond the terminal femoral. However, out of 282 cases, as noted by Pearse, thirty-four came to rest at the bifurcation of the aorta, creating a riding embolus. This particular group presents probably the most fatal type of embolectomy, because it is very difficult to approach the terminal aorta without at least a spinal anesthesia, unless the retrograde procedure of Key is used, and, although this may be successful, it is difficult to see that its success in a riding embolus, such as the case to be reported, would be as good as a direct approach, which was followed in this and previous cases.

The original embolectomy of the aorta through incisions in the right and left common iliac of our patient was followed three days subsequently by embolectomy of the right common femoral at its bifurcation into the profunda and ten days later by a supracondylar amputation of the right limb, which revealed an embolus in the popliteal artery.

CASE REPORT

The patient was a 24-year-old white woman who entered the hospital because of dyspnea, cough, and fever of one week's duration. She had been a known rheumatic since the age of 5 years when she showed manifestation of chorea which lasted for a year. Three years later she developed polyarthritis which necessitated bed rest for two months. At the age of 10 years she had another attack of polyarthritis, and it was at this time that cardiac manifestations were first noted. At the age of 15 years the patient had a third attack of polyarthritis and carditis, and since that time has been on digitalis and limited activity. Dyspnea on exertion has continued despite this medication. For ten days prior to admission the patient had a cough with increase in her dyspnea and, when a temperature of 103° F. appeared, decided to be hospitalized.

Her past history, aside from rheumatic fever, revealed measles, mumps, and chicken pox in childhood, a tonsillectomy at the age of 7 years, and excision of a pilonidal cyst at 18 years of age.

Family History.—Irrelevant.

Physical Examination.—On admission physical examination showed a very acutely ill young white female who was feverish and markedly dyspneic and orthopneic. Temperature, 105.6° F., pulse, 150; respirations, 28; blood pressure, 140/82. Eyes: Pupils equal and reactive; fundi normal; no petechiae. Ears, nose, and throat: Nose, engorged turbinates; ears, negative; mouth, tongue furred, teeth poor, pharynx red. Neck: Veins distended and fill from below, thyroid slightly enlarged. Breasts: No masses. Chest: Coarse moist râles throughout chest; moderate number of fine crepitant râles at both bases. Heart: Apex beat forceful and present in seventh intercostal space at anterior axillary line, systolic thrill at apex, rapid, irregular in rate with pulse deficit, blowing systolic murmur at apex transmitted upward toward base, M_1 loud, P_2 accentuated. Abdomen: Liver four fingers below costal margin and tender; spleen and kidneys not felt. Extremities: No edema, clubbing, cyanosis, or petechiae. Neurologic: Physiologic.

Laboratory Data on Admission.—White blood cells: 13,150 with 84 per cent polymorphonuclears, 13 per cent lymphocytes, and 3 per cent monocytes. Red blood cells: 4.4 million with 75 per cent hemoglobin (Sahli). Sedimentation Time: Twenty minutes for 18 mm. Urine: Yellow, 1020, acid, one plus albumin; sugar, acetone, and microscopic negative. Wassermann: Negative. Blood Chemistry: Sugar, 117.6 mg. per cent; urea nitrogen, 11.9 mg. per cent. Blood Culture: Negative 3/18, 3/19, 3/20, 3/21, 3/22, 3/30. Sputum: Pneumococcus type 18. Electrocardiogram: Myocardial damage, auricular fibrillation, right deviation electrical axis. Chest Plate: Heart of characteristic mitral configuration, markedly enlarged (cardiothoracic ratio 0.73); lung fields show marked congestion secondary to cardiac decompensation.

Course.—The patient was desperately ill on admission to the hospital. It was felt that she had rheumatic heart disease with rapid auricular fibrillation and decompensation and probably bronchopneumonia. She was given 5 cat units of digifolin intravenously, 5 cat units intramuscularly, and later 4 cat units of digitalis leaf orally. Morphine, oxygen, and 50 per cent glucose intravenously were administered. Sodium sulfapyridine, 4 Gm. intravenously, were given immediately and sulfathiazole started at 1 Gm. every four hours orally after an initial dose of 3 Gm.

On this regime the patient's improvement was remarkable; her temperature fell to normal, and her fibrillation was well controlled. On the evening of March 28, ten days after admission, she complained of sudden cramplike pains in both legs from the hips down and pain low in the back, followed by a sensation of heat and then numbness. Examination showed both legs from the hips down to be cool, slightly cyanotic, and hypesthetic. Femoral, popliteal, and dorsalis pedis pulses could not be felt, and oscillometric readings were zero. A diagnosis of saddle embolus at the bifurcation of the aorta was made and surgical consultation requested. The diagnosis was confirmed and decision made to operate immediately. Meanwhile, a cradle had been put over both legs with temperature at 90° F., the legs were oiled and bound with cotton, papaverine, ½ gr., and atropine sulfate, 1/150 gr., were given intravenously; morphine sulfate, 1/6 gr., subcutaneously; papaverine, 1 gr., whiskey, ½ oz., and nicotinic acid, 100 mg., given orally.

She was operated upon four hours following the onset of the pain. Under spinal anesthesia, a midline lower abdominal incision was made. Intestines were pushed back out of the pelvis and above the sacral promontory. The retroperitoneal space was opened and the terminal aorta with its bifurcation exposed. The bifurcation was found at the body of the third lumbar vertebra. About 2 cm. above this level the inferior mesenteric had its origin. There was pulsation down to within 1½ cm. of the bifurcation. No pulsation was noted at the bifurcation or in the right and left common iliacs. The terminal aorta was ligated. Perivascular coats were dissected from the common iliacs. Left common iliac was incised anteriorly for a distance of about 1 cm., and, upon incising the intima, an embolus was noted

protruding through the incision. This was gently removed with forceps and found to be about 6 cm. in length. There was a fair quantity and continuous reflux of blood from below this point. The opening in the vessel was closed with interrupted No. 6-0 oiled silk sutures. A cuff of peritoneum was placed around the incised part of the artery with endothelial side next to the vessel. A small leak of reflux blood necessitated two more interrupted sutures at the point of arterial opening. The right common iliac was then opened at the same level, about 1½ cm. below the bifurcation. Incision in the vessel was the same length as the one on the left. As the intima was opened, an organized embolus extruded through the opening. This was slowly removed as on the previous side. Examination of the embolus showed that the distal part was apparently missing, and the embolus came out in three pieces. A catheter with suction was applied up the proximal part of the

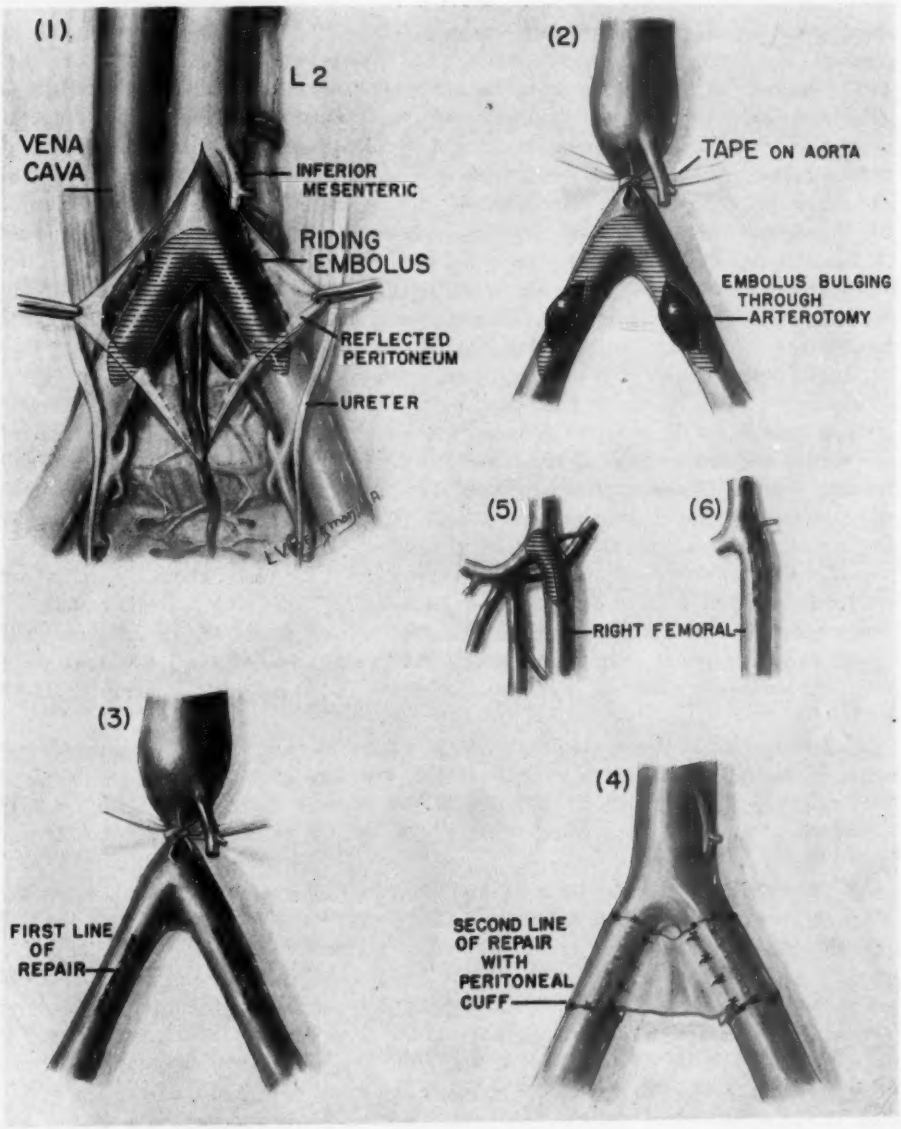

Fig. 1.—(*1*) Anatomical exposure: (*2*) compression of aorta and bilateral arterotomy; (*3*) and (*4*) first and second line of repair—note peritoneal cuff; (*5*) and (*6*) femoral arterotomy with mattress closure after embolectomy.

right common iliac, and two or three small pieces of friable embolus were removed from the bifurcation and up to the level of the ligature on the aorta. The catheter with suction was then inserted down into the distal part of the right common iliac for a distance of about 10 to 12 cm., and suction was applied, but no organized embolus could be withdrawn. The opening in the vessel was closed with interrupted No. 6-0 oiled silk. A flap of peritoneum was sutured over the opening in the vessel. It was noted that when the right vessel was opened, there was very little reflux of blood from below. After the opening in the common iliac had been thoroughly closed, the ligature was removed from the terminal aorta. There was no evidence of pulsation below the point at which the terminal aorta had been ligated. The patient's legs and feet were examined at this time, and, although there was definite improvement in the warmth of the left foot and leg, there was no evidence of pulsation in the tibial or femoral arteries. There was slight improvement in the right leg as far as warmth was concerned by the time the operation was completed. The retroperitoneal space opening was closed with continuous atraumatic No. 1. The abdomen was closed in layers.

The patient withstood the operation remarkably well. Additional digitalis was given preoperatively, and the fibrillation was well controlled throughout the operation at a rate below 100 per minute.

The following day the patient's legs were warmer and less cyanotic. Sensation and motor power in the legs improved. The left femoral pulsation was palpable but not the right. Oscillometric readings lower down were still zero. During the course of the next few days the left leg improved even further and an oscillometric reading of ½ was obtained in the entire leg. The right leg remained cool, pale, and slightly cyanotic. The right femoral pulsation was absent, and no oscillometric reading could be obtained in the right leg. It was decided to explore the right femoral artery and on April 1, three days following the first operation, the patient was taken to the operating room where, under 2 per cent novocain infiltration anesthesia, a transverse incision parallel to the inguinal ligament was made over the falx inguinale. Femoral artery was exposed and found to branch at this level into the profundi femoral and femoral artery. These arteries were opened separately and a No. 9 catheter inserted for a distance of 40 cm. upward and 40 cm. downward from the point of incision in the vessel. Suction was applied in each instance. The catheter was gradually removed. A small organized embolus was removed from the vessel about 3½ cm. above its bifurcation. No other emboli could be found. There was a small amount of reflux blood flow with a very weak pulsation following removal of this embolus. The openings in the vessel were closed with two rows of No. 6-0 oiled silk continuous mattress sutures. Skin and fascia were closed in layers with interrupted black silk.

Following this operation, the right thigh became warmer, the color improved, and an oscillometric reading of ½ was obtained. The portion below the knee remained cool and slightly cyanotic. In addition to the medical therapy previously outlined (intravenous and oral papaverine, whiskey, heat cradle, sedation), a pavex boot was also added.

By April 6 the patient was alert and cheerful and greatly improved. Her left leg was warm and had good femoral pulsation. She could move this leg readily and had no complaints referable to it. The right leg was warm down to the knee but slightly cool and cyanotic below this point. She could move the leg, but complained of frequent pain in the calf and foot. By April 10, nine days following the femoral exploration, the patient was running a low-grade fever ranging around 101° F., and it was obvious that the lower third of the right leg was becoming gangrenous and amputation was decided upon. The following day, under spinal anesthesia, a supracondylar amputation of the right thigh was performed. Anterior and posterior flap incisions were made through skin, fascia, and muscles. The femoral vein and artery were clamped and cut and the femur was sawed through. The femoral artery was

opened and a No. 9 catheter with suction was applied and fed up into the artery for a distance of about 3 cm. A well-organized embolus about 1.5 cm. in length was removed with a small artery forceps. The artery was then incised for a distance of about 3 cm. and a metal eustachian catheter was inserted for its full length into it. Suction was applied and the catheter gradually removed. There was no pulsation in the vessel, and only a small quantity of arterial blood seemed to come down from it, but in an amount sufficient to necessitate ligating the end of the vessel. The sciatic nerve was retracted downward, injected with absolute alcohol, and about 3 cm. excised. Muscles over the stump of the bone were brought together by interrupted chromic sutures. Skin was closed with interrupted black silk.

Following this operation, the patient rapidly improved and was soon able to get about in a wheel chair. After about a week she started to run a low-grade fever and examination revealed a recurrent infected pilonidal cyst. This was drained *(Bacillus coli)*, irrigated, and packed with sulfathiazole. Improvement was noted in the patient's general condition for several days but later began to show more dyspnea and orthopnea than usual. She responded poorly to the usual medical measures. On her twenty-seventh hospital day she was extremely dyspneic, and coarse râles were heard throughout the chest. She responded temporarily to morphine, oxygen, 50 per cent glucose intravenously, and digitalis, but that evening suddenly started to scream, complained of severe pain in the chest, and died within a few minutes.

SUMMARY

Although the patient died twenty-seven days postoperatively from what was apparently pulmonary infarction, we feel that the case is of sufficient interest to be reported because it does prove again that patients with severe cardiac conditions can be subjected to major surgical procedures without immediate mortality.

Autopsy would have made the case complete, and we regret that we are not able to give such a report. However, in summary, (1) a case of riding embolus at the bifurcation of the aorta is reported; (2) the patient withstood three major surgical procedures in spite of the fact that she had a severe cardiac condition; and (3) technique of embolectomy has been illustrated.

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CENTENNIAL OF CRAWFORD LONG'S FIRST USE OF ETHER IN SURGERY

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IT HAS been said that medicine has advanced more in the last hundred years than in all other times combined. Such a statement appears to be particularly accurate in the year 1942, since the first surgical anesthetic was administered just one hundred years ago, March 30, 1842. Then followed the epochal pioneer work of Pasteur, Lister, Koch, Roentgen, Halsted, and others, which has contributed so materially toward creating such an unparalleled hundred years in medicine.

Disagreements over priorities in important discoveries in medicine and other sciences have led to discussions and sometimes heated arguments which have never ended and which will not end so long as there is a single supporter to champion the cause of any claimant. In no debate over priority of discovery in medicine has interest and feeling existed so intensely and so long as in the discovery of surgical anesthesia. There seem to be two main reasons for this situation. If the discovery had been an ordinary one the matter would have been settled promptly and forgotten. But since the finding of means to make painless surgery possible was an achievement eagerly desired and sought throughout the centuries, and since no acquisition in medicine was more valuable, it was natural and human that any claimant to the immortal honor would press his demands vigorously, or have them so presented by his advocates. Another reason for the war of words and pamphlets which has existed over the discovery of anesthesia was the fact that all the contestants in the drama played their roles in a period of less than five years. If the different events had been distributed over longer time, and had most of the claimants not known one another and had not been brought into actual contact with one another, the violence of the controversy would have been less marked and sooner forgotten.

It is not the purpose of the present paper to reopen the discussion, but to describe the part taken by one of the participants, Crawford Williamson Long, in commemoration of the centennial of his achievement. As a matter of fact, the name of Crawford Long did not figure conspicuously in the famous "ether controversy." The heated arguments were mainly between the New England contenders and their supporters, Horace Wells, of Hartford, and W. T. G. Morton and Charles T. Jackson, of Boston.

One of the most frequently quoted axioms of Louis Pasteur reads, "In the realm of observation, chance only favors the mind prepared." What preparation had Crawford Long which led him by chance to make such a useful discovery? Many of the world's greatest men have arisen

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from the humblest, most unpromising origins. It has been thought by some that Long possessed but little education and training, which was true of most medical practitioners of a century ago. But such was not the case with Dr. Long. Judged by modern standards which require that animal experimentation should precede clinical application in medical studies, Long did not appear to be prepared to produce such a monumental discovery, but he did possess a trained background and keen intellect which enabled him to make careful observations and appreciate their significance.

ANCESTRY AND PREPARATION

He was born in Danielsville, Madison County, Georgia, Nov. 1, 1815. His grandfather was Captain Samuel Long, Irish by birth, who emigrated to Pennsylvania in 1762, and settled in Carlisle, marrying Miss Williamson, of Ulster, Ireland. He served in the army of Washington, and at the Yorktown surrender was a captain in the command of the Marquis de Lafayette. After the war, in 1792, Samuel Long moved to Madison County, Georgia, taking with him his 11-year-old son, James, who had been born in Carlisle. This James Long, father of Crawford, married Elizabeth Ware, a Virginia girl, whose parents were born and reared in Albemarle County, Virginia, and had come to Georgia and settled in Madison County. She was an energetic, warm-hearted, ambitious woman, of refined taste and much literary ability. Crawford's father was a planter, and for years was clerk of the Supreme Court. He sat in the state senate for two terms and was the intimate and trusted friend of the Georgia statesman, William H. Crawford, who was successively United States senator, minister to France, secretary of the treasury, and candidate for President of the United States, in 1824, against John Quincy Adams, Andrew Jackson, and Henry Clay. Dr. Long was named after William H. Crawford and Captain Samuel Long's wife.

Crawford attended the academy in his native town, and at the age of 14 years entered Franklin College, now the University of Georgia, where he took the degree of master of arts, in 1835, at the age of 19, being considered "studious and wise" beyond his years, and called "the Baby" at college because of his youth. He stood second in the graduating class. Contemporaneous with him were several distinguished Georgians: General Howell Cobb; General Benning, of Columbus, after whom Fort Benning is named; Senator Herschel V. Johnson; General Francis Bartow, of Savannah, who was killed at the First Battle of Manassas; and Senator A. O. Bacon. His roommate and closest friend, however, was Alexander H. Stephens, who became vice-president of the Confederacy. It is remarkable that two college roommates should have been chosen as the two illustrious citizens to represent Georgia in the National Statuary Hall. Undoubtedly the embryo physician must have received inspiration for his future success by his association with such men as these, as they must have felt the stimulation of contact with him.

Long taught for one year in the Danielsville Academy, and after that began the study of medicine at Jefferson, Georgia, under Dr. Grant. He then took a medical course of one year at Transylvania College, at Lexington, Kentucky, which was the second medical school to be organized in this country, Pennsylvania being the first. He reached this distant place by riding horseback over the mountains, with his rifle in his lap, because this section was still infested with Indians who often were on the warpath.

In 1837, he entered the medical department of the University of Pennsylvania, which was then, as today, one of the leading medical schools of the world. Philip Syng Physick, pupil of John Hunter, and father of American surgery, died during Long's first course. William Gibson, pupil of Sir Charles Bell, succeeded Physick as professor of surgery. While traveling in Europe Physick had been present as a spectator at the battle of Waterloo, and was wounded by a stray bullet. He is said to have been the first man to tie the common iliac artery (1812). Nathaniel Chapman was professor of practice of physic and clinical medicine; George B. Wood taught materia medica; William E. Horner, discoverer of the tensor tarsi, was professor of anatomy; Hugh L. Hodge, who invented pessaries and obstetrical forceps, was professor of midwifery; and Robert Hare was the celebrated professor of chemistry. A medical student of this time could hardly have been taught by a more capable faculty.

Receiving the degree of M.D. from Pennsylvania University in 1839, he next went to New York, where he spent eighteen months "walking the hospitals." The extent of postgraduate training offered by this course is not stated, but it was the best that could be obtained in the United States at this period. Among those whom he had opportunity to hear were Valentine Mott, Kearney Rogers, and Willard Parker. From filial duty young Long felt obliged to return home to practice. Had he elected to locate in New York or Philadelphia, as he once decided to do, and could have administered ether for the first time in such a large center, the question of priority in the discovery would not have arisen and have caused such acrimonious discussions.

In 1841, at 26 years of age, Dr. Long settled in the little town of Jefferson, Jackson County, Georgia, buying out the practice of his old preceptor, Dr. Grant. He soon acquired a lucrative practice, which grew rapidly and extended into the neighboring counties and towns of Georgia. His house in the village became the favorite social resort for the young men of the vicinity, and it was here that the discovery of ether anesthesia was made, March 30, 1842.

On August 11, 1842, Dr. Long married Mary Caroline Swain, the 16-year-old daughter of a planter, George Swain, and the niece of Governor Swain, of North Carolina, who was afterward president of the University of North Carolina. She was a lovely and intellectual woman, fit in every way to be the life partner of such a man. Mrs. Long died

September 22, 1888, at Comfort, Texas, from injuries received in a railroad wreck. She lies buried with her husband in Oconee Hill Cemetery at Athens. Twelve children were born to this marriage; six grew to maturity. The last surviving child, Mrs. Eugenia Long Harper, died July 5, 1940. Two grandchildren are alive, and great- and great-great-grandchildren.

It is interesting to note that for one year, in 1850-51, Dr. Long lived in the budding city of Atlanta, but he found it a rather rough railroad town, with so little promise that he moved to the classic city of Athens, where there were better advantages for educating his children. He continued to reside in Athens until the day of his death, June 16, 1878, after practicing medicine for nearly forty years. A recent writer said that Crawford Long "died in obscurity." Nothing could be further from the truth. When he died the whole state mourned and greater tributes of praise were never showered upon a citizen of Georgia.

EMINENT ON MANY COUNTS

Even without being the first to use anesthesia, Dr. Long would be considered one of Georgia's most distinguished physicians. At the unveiling of the monument to his memory in 1912, in Jefferson, Dr. Woods Hutchinson said that Long was in many respects in advance of his day. He treated and cured consumption by food and fresh air, and he treated typhoid fever as it was treated in 1912. He operated several times successfully for cancer of the breast, always clearing the ribs and removing the axillary glands. He is said to have cured several cases of lockjaw and was especially skilled in the use of obstetrical forceps.

Long was reared a Presbyterian, his father and paternal grandfather having been elders in the Presbyterian Church, but he joined the Methodist Church in order to be with his wife. He considered slavery as God's method of civilizing the African, and felt deeply the responsibility of having slaves to control and influence. Politically he was a Whig, and with his friend, Alexander H. Stephens, he opposed secession, but like many other patriots, he "went with his state."

During the War Between the States he did not join the enlisted forces, but was appointed by the Confederate government in charge of the military hospital on the university campus at Athens, where he rendered valuable service. The Southern Cross of Honor was conferred upon him by the United Daughters of the Confederacy.

All who knew him unite in declaring him a man of exceptional qualities of mind and soul. Dignified in manner, his whole appearance betokened culture and high character. He was sensitive, refined, and considerate of others, free from envy, malice, and uncharitableness. He maintained a slight reserve, except among intimates and congenial people. Cheerful in the sick room, he inspired his patients with confidence. He was fond of Shakespeare and good music; he was tall and slender, dressed in conventional black, always with frock coat, usually made by

a New York tailor; in short, he was a high-bred, scholarly, Christian gentleman.

BEFORE ANESTHESIA

In 1799, Sir Humphrey Davy, the English chemist, announced that the inhalation of nitrous oxide gas would produce insensibility and had cured toothache, adding these significant words, "As nitrous oxide appears capable of destroying pain it may probably be used with advantage during surgical operations." Here he stood upon the very threshold of the wonderful discovery, but Davy was not a medical man, and none was found progressive enough to carry out his suggestion.

Sulphuric ether had been known for a long time as a chemical agent, but it was regarded as too dangerous to be used in medicine. Between the years 1795 and 1839, however, different experimenters, such as Pareira and Faraday in England, Thomson in Scotland, and Godwin, Wood, and others in America, showed that the vapor of ether when inhaled would produce effects similar to those of nitrous oxide gas, such as exhilaration, excitement, laughter, crying, and insensibility, and would relieve the spasmodic disorders of colic, asthma, and whooping cough, and would cause insensibility to pain. And yet no one had the courage to employ ether in surgery or obstetrics. As late as 1839, Velpeau, the famous French surgeon, declared, "To escape pain in surgical operations is a chimera which we are not permitted to look for in our day."

During the first half of the nineteenth century there was an odd class of persons who traveled about the country, first in England and later in the United States, lecturing in public on chemistry. One of the features of the program was to invite certain members of the audience upon the stage to inhale nitrous oxide or ether vapor "for the purpose of provoking exhilaration, excitement, semiconscious gyrations, and mirth-producing antics for the amusement of the spectators." This first began with the use of nitrous oxide, but soon ether became the favorite for the reason that it was more easily manipulated. From these strange entertainments evolved the so-called ether parties, or "frolics," which became popular throughout the country.

Here it is appropriate to insert Dr. Long's own account of how he came to give the first anesthetic for a surgical operation, describing his first cases. This statement was read before the Medical Association of Georgia, in 1852.

FIRST OPERATION WITH ETHER

In the Southern Medical and Surgical Journal for December, 1849, I presented an account of what I considered the first use of ether by inhalation as an anesthetic agent in surgical operations; a summary of which I will proceed to read to the Medical Association of Georgia.

Previous to stating the first operation performed by me with ether, I will briefly give the reasons which induced me to make experiments in etherization. In the month of December, 1841, or January, 1842, the subject of the inhalation of nitrous oxide gas was introduced in a company of young men

assembled at night in the village of Jefferson, Ga., and the party requested me to prepare them some. I informed them that I had not the requisite apparatus for preparing or using the gas, but that I had an article (sulphuric ether) which would produce equally exhilarating effects and was as safe. The company was anxious to witness its effects; the ether was produced, and all present in turn, inhaled. They were so much pleased with its effects that they afterwards frequently used it and induced others to use it, and the practice became quite fashionable in the county and some of the contiguous counties. On numerous occasions I inhaled the ether for its exhilarating properties and would frequently at some short time subsequently discover bruises or painful spots on my person which I had no recollection of causing and which I felt satisfied were received while under the influence of ether. I noticed my friends, while etherized, received falls and blows which I believed were sufficient to cause pain on a person not in a state of anesthesia, and on questioning them they uniformly assured me they did not feel the least pain from these accidents.

Observing these facts I was led to believe that anesthesia was produced by the inhalation of ether and that its use would be applicable in surgical operations.

The first person to whom I administered ether in a surgical operation was Mr. James M. Venable, who then resided within two miles of Jefferson, and at the present time in Cobb County, Georgia. Mr. Venable consulted me on several occasions as to the propriety of removing two small tumors on the back part of his neck, but would postpone from time to time having the operation performed from dread of pain. At length I mentioned to him the fact of my receiving bruises while under the influence of the vapor of ether, without suffering, and, as I knew him to be fond of and accustomed to inhale ether, I suggested to him the probability that the operation might be performed without pain, and suggested to him operating while he was under its influence. He consented to have one tumor removed, and the operation was performed the same evening. The ether was given to Mr. Venable on a towel and when fully under its influence, I extirpated the tumor. It was encysted and about one-half an inch in diameter. The patient continued to inhale ether during the time of the operation, and seemed incredulous until the tumor was shown to him. He gave no evidence of pain during the operation and assured me after it was over that he did not experience the least degree of pain from its performance. This operation was performed on March 30, 1842.

The second operation I performed on a patient etherized was on the sixth of June, 1842, and was on the same person for the removal of the other tumor. This operation required more time than the first from the cyst of the tumor having formed adhesions to the adjoining parts. The patient was insensible to pain during the operation until the last attachment of the cyst of the tumor was separated, when he exhibited signs of slight suffering, but asserted, after the operation was over, that the sensation of pain was so slight as scarcely to be perceived. In this operation the inhalation of ether ceased before the first incision was made. Since that time I have invariably desired patients, when practicable, to continue the inhalation during the time of the operation.

Having permitted such a time to elapse without making public my experiments in etherization [the author stated that these operations were made known to physicians and the people all about Jefferson and Athens at the time they occurred], in order to show the correctness of my statements, I procured the certificate of the patient on whom the first operation was performed,

the certificates of two who were present at the time of the operation, and also of his mother, brothers and sisters and a number of his immediate friends who heard him speak of the operations soon after they were performed.

Fig. 1.—Portrait of oil painting of Crawford W. Long by Lewis Gregg.

THE FACTS CERTIFIED

The Southern Medical and Surgical Journal of 1849, December, contained but two of the certificates. I have a number of others which may be seen or read, if desired by the association.

My third case was a negro boy who had a disease of the toe which rendered amputation necessary, and the operation was performed July 3, 1842, without the boy evincing the slightest degree of pain.

These were all the surgical operations performed by me in the year 1842 upon patients etherized, no other cases occurring in which I believed the inhalation of ether applicable. Since 1842 I have performed one or more operations, annually, on patients in a state of etherization. I procured some certificates in regard to these operations, but not with the same particularity as in regard to the first operations, my sole object being to establish my claim to priority of discovery of the power of ether to produce anesthesia. However, these certificates can be examined.

The reason which influenced me in not publishing earlier, I was anxious before making my publication to try etherization in a sufficient number of cases to fully satisfy my mind that anesthesia was produced by the ether and was not the effect of the imagination, or owing to any peculiar insusceptibility to pain in the persons experimented on.

At the time I was experimenting with ether, there were physicians "high in authority" who were the advocates of "mesmerism," and recommended the induction of the mesmeric state as adequate to prevent pain in surgical operations. Not withstanding thus sanctioned, I was an unbeliever in the "science," and was of the opinion that if the mesmeric state could be produced at all, it was only on those of strong imagination and weak minds, and was to be ascribed solely to the working of the patient's imagination. Entertaining this opinion, I was the more particular in my experiments in etherization.

Surgical operations are not of frequent occurrence in a country practice, and especially in the practice of a young physician; yet I was fortunate enough to meet with two cases in which I could satisfactorily test the anesthetic powers of ether. From one of these patients I removed three tumors the same day; the inhalation of ether was used only in the second operation and was effectual in preventing pain, while the patient suffered severely from the extirpation of the other two tumors.

In another case I amputated two fingers of a negro boy; the boy being etherized during the operation as to one finger and not during the other—he suffered during the operation as to one finger and not during the other. After fully satisfying myself of the power of ether to produce anesthesia, I was desirous of administering it in a severer surgical operation than any I had performed. In my practice prior to the published account of the use of ether as an anesthetic I had no opportunity of experimenting with it in a capital operation, my cases being confined, with one exception, to excising small tumors and the amputation of fingers and toes. While cautiously experimenting with ether as cases occurred, with the view of testing its anesthetic powers and its applicability to severe as well as minor surgical operations, others, more favorably situated, engaged in similar experiments and consequently the publication of etherization did not "bide my time." I know that I deferred the publication too long to receive any honor from the priority of the discovery, but having by the persuasion of friends presented my claims before the profession, I prefer that its correctness be fully investigated before the medical society. Should the society say that the claim, though well founded, is forfeited by not being presented earlier, I will cheerfully respond: "So mote it be."

Not wishing to intrude upon the time of the association, I have made this short compendium of all the material points stated in my article in the Journal; and if the society wishes any further information on the subject I will cheerfully comply with their wishes.

(Signed) C. W. Long, M.D.

FURTHER PROOFS

Following the reading of the foregoing paper the Association (See Transactions, pp. 113-117) unanimously passed the following resolution:

> Resolved, That this society is of the opinion that Dr. Crawford W. Long was the first person who used sulphuric ether as an anesthetic in operations, and as an act of justice to him individually and to the honor of the profession of our own state, we most earnestly recommend him to present at once his claims to priority in the use of this most important agent to the consideration of the American Medical Association at its next meeting, Dr. Dickinson, Dr. Cooper, Dr. S. N. Harris, committee.

Mr. Venable's story of the first anesthetic is given in the following affidavit:

> I, James M. Venable, of the county of Cobb and state of Georgia, on oath depose and say, that in 1842 I resided at my mother's in Jackson County, about two miles from the village of Jefferson, and attended the village academy that year.
>
> In the early part of the year the young men of Jefferson and the country adjoining were in the habit of inhaling ether for its exhilarating powers, and I inhaled it frequently for that purpose, and was very fond of its use.
>
> While attending the academy I was frequently in the office of Dr. C. W. Long, and having two tumors on the back of my neck, I several times spoke to him about the propriety of cutting them out, but postponed the operation from time to time. On one occasion we had some conversation about the probability that the tumors might be cut out while I was under the influence of sulphuric ether, without my experiencing pain, and he proposed operating on me while under its influence.
>
> I agreed to have one tumor cut out and had the operation performed that evening after school was dismissed. This was in the early part of the spring of 1842.
>
> I commenced inhaling the ether before the operation was commenced and continued it until the operation was over. I did not believe the tumor was removed until it was shown to me.
>
> A month or two after this time, Dr. C. W. Long cut out the other tumor, situated on the same side of my neck. In this operation I did not feel the least pain until the last cut was made, when I felt a little pain. In this operation I stopped inhaling the ether before the operation was finished.
>
> I inhaled the ether in both cases, from a towel, which was the common method of taking it.
>
> James M. Venable.
>
> *(Sworn to before me)* Alfred Manes, J.P.

This operation was done in the presence of four witnesses, James E. Hayes, A. T. Thurmond, W. H. Thurmond, principal of the academy, and Edmond S. Rawls, the last of whom testifies as follows.

> I, Edmond S. Rawls, of Rome, Floyd Co., Ga., on oath depose and say that —on one occasion during that year (1842) I was present with James M. Venable in the office of Dr. C. W. Long, in Jefferson, Jackson Co., Ga., and witnessed Dr. C. W. Long cut out a tumor from the side of neck of J. M. Venable while said Venable was fully under the effects of the vapor sulphuric ether inhaled from a towel, and without his exhibiting the least symptoms of suffering pain from the operation. J. M. Venable was so unconscious of the

operation having been performed that he would not believe the tumor was removed until it was shown him.

(Signed) E. S. Rawls, M.D.
(Sworn to and subscribed before me this second of November, 1853) E. L. Newton, J.J.C.

The opponents of Long's claim to priority in the use of anesthesia say that he kept his discovery a secret and that he, therefore, deserved no credit for it. The next two certificates from Dr. de la Perriere and Dr. Carlton, prominent physicians of the community, show that Long's work was well known to citizens of the town of Jefferson and neighboring places, particularly Athens, the center of learning in Georgia; that it was considered a remarkable discovery by the populace, and that these doctors knew of it and realized its importance:

Georgia, Jackson County.

I, Ange de la Perriere, M.D., do certify that I resided in Jefferson County, Georgia, in the year 1842, and that sometime in that year I heard James M. Venable, then of said county, speak of Dr. C. W. Long's cutting off two tumors from his neck while under the influence of the inhalation of sulphuric ether, without pain or being conscious of the performance of the operation.

I do further certify that the fact of Dr. C. W. Long using sulphuric ether by inhalation to prevent pain in surgical operations was frequently spoken of and notorious to the county of Jackson, Georgia, in the year of 1842.

A. de la Perriere, M.D.
(Sworn to and subscribed before me this thirtieth of March, 1854) N. H. Pendergrass, J.P.

Athens, Clarke Co., Georgia.

I, the undersigned, do certify that in May, 1843, I assisted Dr. R. D. Moore in amputating the leg of a colored boy Augustus, then the property of Mr. Wm. Stroud, who resided in this county; and that I distinctly recollect hearing Dr. R. D. Moore say, "If I had thought of it before leaving home I would have tried Dr. C. W. Long's great discovery, namely the administration of sulphuric ether as an anesthetic in performing the operation." Having neglected to bring the ether, Dr. Moore finally concluded to influence the patient with morphia; under which influence the operation was performed.

Jos. B. Carlton, M.D.

Many other certificates could be offered to prove these facts but these seem sufficient for the present narrative. The original copies of all the documents, affidavits, etc., are now in possession of the Smithsonian Institute, in Washington, D. C. Many distinguished surgeons and other writers have contributed articles on Long's discovery of anesthesia. Among these are J. Marion Sims, Hugh H. Young, John Chalmers da Costa, Dudley W. Buxton, the English anesthetist, Joseph Jacobs, Long's young office boy, and others. The most complete account is given in Mrs. Taylor's work.

If the statements of Crawford Long's daughters are authentic, his use of anesthesia in obstetrics preceded by two years its employment by Sir James Y. Simpson. Mrs. Harper, in a signed letter to the writer,

declared that she and other members of the family had often heard their mother say that Dr. Long administered ether to her at the birth of her second child, who was Mrs. Frances Long Taylor, born Dec. 17, 1845. The family Bible corroborates this date. This important date in the history of anesthesia was not published until after Mrs. Taylor's death. She could have given it as an addition to her father's claim to fame, but in so doing she would divulge her age, which the proud lady was loath to do.

Fig. 2.—Long's first operation under ether. Maurice Siegler.

It has been charged that Long used ether anesthesia only a few times and then abandoned it. In a letter written in 1921, Mrs. Taylor stated that the complete records of her father's operations under ether were lost in 1908, but that at the time she wrote there were living witnesses or their descendents in and around Athens who testified that Dr. Long used ether continuously up to the very day of his death. From memory Mrs. Taylor named fifteen occasions in which ether was employed as an anesthetic, five times in difficult obstetrical cases. The other ten cases included eight breast amputations, one amputation of the leg, and an operation for cancer of the groin. In the breast amputations it is claimed that the axillary glands were removed and the ribs "scraped." Mrs. Taylor also wrote that there were many "minor" operations under ether anesthesia which were not recorded.

The chief argument used against Crawford Long as the discoverer of surgical anesthesia is that he made no publication of his experiments

until December, 1849, three years after the universal publication and adoption of the method. While it is true that Long did not publish his work in a periodical until this date, from the very first he made no secret of the discovery; he always operated in the presence of witnesses, and encouraged publicity by public discussion and by urging the use of ether by other physicians, so that it was known over a wide section of country. The nearest hospital, medical journal, and railroad were at Augusta, 140 miles away, and the nearest newspaper, a weekly, was at Athens, 20 miles away.

Crawford Long has been honored in many ways besides those already mentioned. Various bodies of medical men have adopted resolutions expressing the belief that he is entitled to be called the discoverer of anesthesia. The Southern Medical Association passed such a resolution in 1922. In 1878, Marion Sims presented the state of Georgia with a heroic size oil painting to be hung in the State Capitol. In 1912, the University of Pennsylvania unveiled a medallion to perpetuate the memory of its illustrious alumnus. The same year Dr. (afterwards Governor) L. G. Hardman, of Commerce, Georgia, gave to the town of Jefferson a marble shaft commemorating the deed of its former citizen, and in 1921, a reduplication of the beautiful medallion at the University of Pennsylvania was placed on the campus of the University of Georgia by Dr. Joseph Jacobs, an alumnus of the institution.

The best portrait of Long is the one painted by Lewis Gregg for Alumni Hall at the University of Georgia. The state of Georgia has erected at Danielsville, Long's birthplace, a replica of the statue in Statuary Hall. In 1931, the name of the Davis-Fischer Sanitarium was changed to the Crawford Long Memorial Hospital, the largest private hospital in Atlanta. Every year on March 30, exercises commemorate the discovery of anesthesia as "Crawford Long Day" at the University of Georgia. In 1940, the United States Post Office issued a postage stamp bearing a portrait of Dr. Long. The first sale of this stamp was made the occasion of a memorable celebration at Jefferson, Georgia, April 8, 1940, when Postmaster General James A. Farley presented the first sheet of stamps to Mrs. Eugenia Long Harper, Dr. Long's sole surviving child. On the Centennial day of Long's discovery, March 30, 1942, an admirable play based on the subject was presented in Atlanta and later given in Augusta at the meeting of the Medical Association of Georgia.

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ACUTE DIVERTICULITIS OF THE CECUM

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DURING the past several years we have encountered six cases of acute diverticulitis of the cecum. In reviewing the literature one is amazed to find so few reported cases of the condition. The first case was reported by Patier in 1912, and since then only thirty-one additional cases have appeared in the literature. It is also surprising to find that the standard textbooks of surgery do not mention the condition.

A complete statistical review of the reported cases has not appeared in the literature to date. Because of the marked similarity in the clinical pictures of appendicitis and diverticulitis of the cecum, the apparent difficulty in recognizing the condition at the operating table, and the lack of standardization in treatment of the condition, we felt that a complete analytical study of the disease was indicated.

Diverticula occur throughout the gastrointestinal tract and are found most frequently in the colon. Diverticula of the colon are classified as the true or congenital and the false or acquired types. The congenital or true type is probably a developmental anomaly falling into the same class as a Meckel's diverticulum. The wall of the true diverticulum contains all the layers of the normal intestinal coat. The false or acquired diverticulum is believed by most writers to be formed as a result of a localized area of weakness in the intestinal wall, combined with a tendency toward constipation and an increased intracolonic pressure. The false diverticula show the absence of one or more muscular layers. True diverticula are almost always found in the region of the cecum and are characteristically single. (See Fig. 1.) False diverticula are almost always multiple and are found most frequently in the rectosigmoid region; they show a decreased incidence from left to right. Both the true and the false diverticula are often asymptomatic, but with the onset of acute inflammation they give rise to acute abdominal signs and symptoms. Thus, true solitary diverticula of the cecum may give rise to acute signs and symptoms in the right lower quadrant.

The thirty-two reported cases of acute diverticulitis of the cecum, together with the six cases treated in our clinic make up the series for the study in this communication. We realize the number of cases is necessarily small but we do feel that a statistical study of the series does bring out several pertinent points.

Acute diverticulitis of the cecum occurs with almost equal frequency in the two sexes with 57.8 per cent of the cases present in females.

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The average age is 40.2 years with 47.3 per cent occurring between the ages of 20 and 40 and 47.3 per cent occurring after the age of 40. Two cases were under 20 years of age. This in itself tends to segregate the condition from the more common condition of multiple diverticulosis and diverticulitis of the colon which occurs almost exclusively after the age of 40.

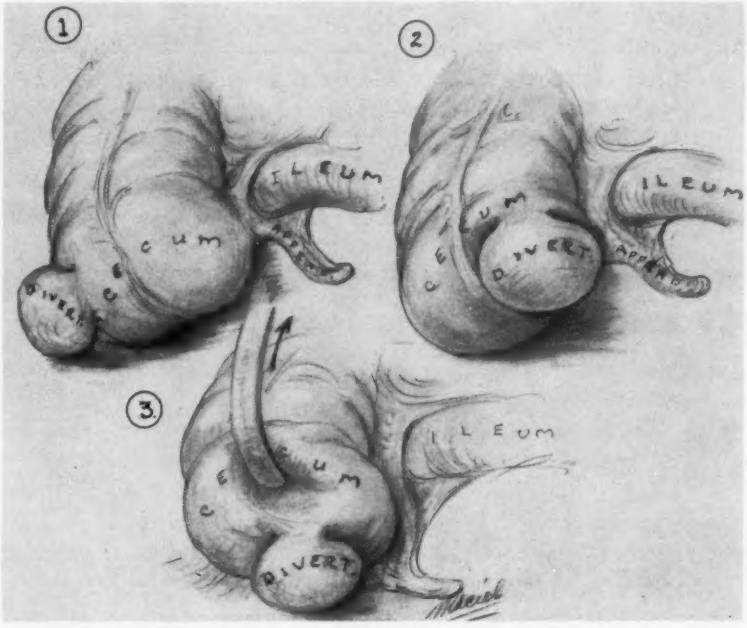

Fig. 1.—The three most common locations of solitary diverticula of the cecum.

The history obtained from a patient with acute diverticulitis of the cecum is very often a typical history for acute appendicitis. Thirty-one and five-tenths per cent of the cases gave a story of epigastric or generalized abdominal pain at the onset with subsequent localization in the right lower quadrant. The duration of pain prior to admission was twenty-four hours or less in 31.5 per cent of the cases, while 55.2 per cent gave a history of pain from one to three days in duration. The patients in 100 per cent of the cases complained of right lower quadrant pain, usually cramping in character. Patients in 44.7 per cent of the cases complained of nausea, while in 26.3 per cent of the cases, vomiting was present.

Examination of the abdomen revealed right lower quadrant tenderness to be present in 97.3 per cent of the cases with associated muscle spasm in 81.5 per cent. A right lower quadrant mass was detected in 26.3 per cent of the patients. The temperatures varied from 98.6 to 102° F., with an average of 99.6. White blood count varied from 6,000 to 22,500 with an average of 12,700. Patients in 23.6 per cent of the cases gave a history of one or more previous attacks.

A preoperative diagnosis of acute appendicitis was made in 68.4 per cent of the cases. This is, of course, the logical diagnosis in a patient with such a history and such clinical findings. A comparison of the pertinent points in the history and findings in acute diverticulitis of the cecum to those in appendicitis as compiled by Reid, Poer, and Merrell reveals the striking similarity of the clinical picture in the two conditions (Table I). In one case the correct diagnosis of acute diverticulitis of the cecum was made before operation. A diagnosis of appendical abscess was made in four cases and the remainder of the diagnoses included intestinal obstruction, abscess of unknown etiology, etc. In none of the cases was a diagnosis of carcinoma of the cecum made preoperatively.

TABLE I

COMPARISON OF THE FINDINGS IN ACUTE DIVERTICULITIS OF THE CECUM AND ACUTE APPENDICITIS

	ACUTE APPENDICITIS	ACUTE DIVERTICULITIS
Sex	66% Male	57.8% Female
Age 11 to 30 inclusive	68%	2 under 40 47.3% (20-40) 47.3% over 40
Typical history of acute appendicitis	53%	31.5%
Nausea	78%	44.7%
Vomiting	73%	26.3%
Pain	94%	100.0%
W.B.C. (Average)	17,200	12,700
Temperature (Average)	100.0° F.	99.6° F.

The diagnosis of the condition at the operating table with the pathology exposed is often quite difficult. In 63.4 per cent of the cases the condition was recognized after the abdomen had been opened.

Five of the cases were diagnosed carcinoma of the cecum; three, tuberculosis of the cecum; two, benign ulcer of the cecum, and in three the interpretation of the lesion at the operating table was not recorded. The lesion is most frequently located on the lateral and anterior aspect of the cecum, but did occur on the medial or posterior aspect of the cecum as well. The condition often develops into a large, firm, indurated mass involving the cecum, which does appear not unlike a malignant lesion. This similarity to carcinoma in gross appearance at least partly explains the high percentage of cases in which radical methods of treatment were used. Patients in 34.2 per cent of the 37 cases operated upon had a right colectomy and ileocolostomy performed upon them. Subsequent pathologic studies of the specimens revealed an inflamed diverticulum of the cecum with an associated typhlitis and pericecal inflammatory mass.

In 52.6 per cent of the cases the condition was recognized and an excision of the diverticulum was done. In three cases the condition was recognized but left undisturbed and an appendectomy was done. In one case drainage only was done. In one instance the condition was

diagnosed clinically and treated conservatively. The patient made an uncomplicated recovery and the cecal diverticulum was revealed in a follow-up barium enema. The tissue was studied in those cases in which an excision and closure or resection was done and all the specimens showed an acute inflammation in the wall of the diverticulum. Some contained fecaliths but many did not. Follow-up barium enemas were done in thirteen of the cases. Nine of the cases showed normal colons; two showed the diverticulum of the cecum and two showed multiple diverticula of the left colon.

In this series of thirty-eight cases there were two deaths, giving a mortality rate of 5.26 per cent, which is much better than one would expect when thirteen of the cases were subjected to a radical resection and anastomoses. One of the deaths occurred in a patient who was subjected to a resection and anastomosis. The other death occurred in one of the patients in whom only drainage had been instituted.

CASE REPORTS

CASE 1.—D. G., a 59-year-old white man was admitted to the hospital, on April 8, 1929. Eight hours before admission the patient developed cramping right lower quadrant pain which persisted and increased in severity. He had no nausea or vomiting and his bowels moved normally the day of the onset. No history of previous similar attacks was obtained.

Positive findings on examination were limited to the abdomen. There was moderate right lower quadrant tenderness with no muscle spasm or rebound tenderness. No mass was palpable. Rectal examination was not recorded; temperature was 98.6° F.; W. B. C., 9,800; urine, negative. The preoperative diagnosis was acute appendicitis.

The patient was explored through a McBurney incision and the cecum was found involved with a hard indurated mass. The lesion was diagnosed as a carcinoma of the cecum. A right rectus incision was made and a right colectomy and ileotransverse colostomy was performed. The patient made an uneventful recovery. Pathologic studies of the specimen revealed the lesion to be an acutely inflamed diverticulum of the cecum with an associated typhlitis. No evidence of carcinoma was found in the sections.

CASE 2.—A white man, aged 30 years, was admitted to the hospital on Oct. 25, 1937. Two weeks before admission this patient had an attack of upper abdominal pain associated with nausea. The attack lasted only two hours and was not associated with right lower quadrant pain or vomiting. Four days before admission the patient developed a similar crampy upper abdominal pain which the night before admission shifted to the right lower quadrant. Nausea was present but the patient did not vomit. He was somewhat constipated and took a cathartic the day before admission. The patient denied any previous similar attacks.

Examination revealed nothing remarkable other than the abdominal and rectal findings. There was slight fullness in the right lower quadrant with a suggestion of a mass in the right iliac fossa. Tenderness was moderate in the right lower quadrant associated with some spasm. In addition there was definite rebound tenderness and pain on coughing both referred to the right lower quadrant. Rectal examination revealed moderate tenderness high on the right; W. B. C., 18,500; urine negative; and temperature, 98.6° F. The preoperative diagnosis was acute appendicitis.

The patient was operated upon through a McBurney incision and on the anterior cecal wall 3 cm. above the ileocecal junction an indurated, inflammatory mass 2 by 2½ cm. was found. The mass was carefully dissected free from the bowel until a small neck was exposed which communicated with the lumen of the bowel. The mass was excised and the remaining defect was closed with purse-string sutures. The appendix was removed. The inverted area of the cecal wall was marsupialized and a protective wick was placed down to the area and the wound closed loosely. Pathologic studies revealed an acute inflammatory reaction in the wall of the diverticulum.

The patient's postoperative course was uneventful and he was discharged on his thirteenth postoperative day. He was seen in the follow-up clinic and was entirely symptom free. A checkup barium enema was negative.

CASE 3.—H. D., a white man, aged 31 years, was admitted to the hospital Dec. 4, 1937. He gave a history of a vague left abdominal pain beginning twenty-four hours previously. The pain tended to subside and he slept well the night before admission, but when he awoke the next morning he had a catching right lower quadrant pain. The pain was exaggerated by walking and straightening up. He was nauseated but did not vomit and gave a history of constipation preceding the attack. A cathartic was taken the morning of admission and his bowels moved twice without exaggeration of the pain. There was no history of previous attacks.

Physical examination revealed slight injection of nasal mucous membranes and slight redness of the pharynx. The abdomen was of normal contour. There was moderate tenderness in the right lower quadrant without muscle spasm. No rebound tenderness or masses were found and the rectal examination was negative. Temperature was 99.6° F.; W. B. C., 15,200; urine completely negative.

The preoperative diagnosis of acute appendicitis and acute pharyngitis and coryza was made.

The patient was operated upon through a McBurney incision and 2 cm. above the appendix on the anterior cecal wall an inflamed, indurated mass 1½ cm. in diameter was found. The neck was dissected out, ligated, the mass excised, and the stump inverted with a purse-string suture. The appendix was also removed. Pathologic studies of the specimen revealed the lesion to be an acutely inflamed diverticulum of the cecum with an associated typhlitis.

Postoperatively the patient did very well and was discharged on the tenth postoperative day. He was seen in the follow-up clinic two months later and was free of symptoms. A checkup barium enema was done, which was entirely negative.

CASE 4.—H. G., a colored man, aged 29 years, was admitted to the hospital on July 19, 1938. He gave a history of the onset of acute upper abdominal pain twenty-four hours previously, which subsided. Seven hours before admission a cramping right lower quadrant pain appeared, which persisted and increased in severity. The pain was increased by coughing and by movement. There was no associated nausea, vomiting, or constipation. The patient denied any previous similar attacks.

Positive findings on examination were limited to the abdomen. The abdomen was normal in contour. There was moderate tenderness and muscle spasm in the right lower quadrant most marked just lateral to McBurney's point. Definite local and referred rebound tenderness to the area mentioned was present. Peristalsis was normal; rectal examination, negative; temperature, 99.4° F.; W.B.C., 12,700; and urine, negative. The preoperative diagnosis was acute appendicitis.

The patient was operated upon and an acutely inflamed diverticulum was found on the posterior wall of the cecum. The diverticulum was excised and the defect closed. In addition, a normal appendix was removed. The McBurney wound was closed without drainage and the patient made an uneventful recovery. Pathologic studies revealed an acute inflammatory reaction in the wall of the diverticulum.

He was seen one month later and was free of symptoms. A follow-up barium enema revealed a normal colon.

CASE 5.—M. D., a white woman, 66 years of age, was admitted to the hospital on July 12, 1940, complaining of abdominal pain. Twenty-four hours before admission the patient developed a cramping right lower quadrant pain which persisted and gradually increased in severity. There was associated anorexia but no nausea or vomiting. The day of the onset the patient noted constipation and she had no bowel movement the day of admission. She had had a similar attack three years before.

Examination revealed a blood pressure of 160/90. There were occasional coarse rhonchi throughout the lung fields. The abdomen was obese and there was diffuse tenderness and muscle spasm in the right lower quadrant. No mass was palpable and there was no rebound tenderness. Pelvic and rectal examinationes revealed no masses or tenderness. Temperature was 100.0° F.; W.B.C., 9,500; urine showed 1+ albumin. The preoperative diagnosis was acute appendicitis.

The patient was explored through a McBurney incision and the cecum was found involved in an inflamed mass of omentum and fibrinous adhesions. A pericecal abscess was found which was drained with cigarette drains and the wound was closed loosely. The appendix appeared normal and thus was not disturbed.

The patient had a stormy postoperative course, developing cardiac asthma and pneumonia. In spite of all supportive therapy she died on the fourteenth postoperative day.

An autopsy was obtained, which revealed the inflammatory process in the diverticulum and surrounding cecum to have subsided completely. The death was attributed to a bilateral pneumonia and cardiac failure.

CASE 6.—W. H., a white man, aged 47 years, was admitted to the hospital on April 4, 1941, with a complaint of abdominal pain. Twenty-eight hours before admission he noted for the first time a generalized abdominal pain in both lower quadrants which became localized to the right lower quadrant eight hours before admission. He complained of no nausea or vomiting and his bowels had moved normally. The patient denied any previous similar attacks.

The positive findings on examination were limited to the abdomen, which was normal in contour. There was moderate tenderness and slight muscle spasm in the right lower quadrant, fairly well localized to McBurney's region. There was also local and referred rebound tenderness to that region. No mass was palpable and peristalsis was active. Rectal examination was negative; temperature, 99.0° F.; W.B.C., 12,700; and urine negative. The preoperative diagnosis was acute appendicitis.

The patient was operated upon through a McBurney incision and an acutely inflamed diverticulum was found on the lateral wall of the cecum. A normal appendix was found which was removed. The diverticulum was left undisturbed and the McBurney incision was closed without drainage. The patient's postoperative course was uneventful and he was discharged from the hospital free of symptoms and in good condition. A follow-up barium enema was not done.

COMMENT

Concerning the treatment of acute cecal diverticulitis it is obvious that a resection and anastomosis is an unnecessary radical procedure which is done as a result of a mistake in diagnosis at the operating table. One must admit that recognition of the condition is often very difficult but there are several definite aids in making the diagnosis.

The majority of the cases occur in patients under the age of 40 and give a fairly characteristic history which closely simulates the history of acute appendicitis. One-third of the patients have had previous attacks. In those cases which have developed large inflammatory masses palpation of the cecal wall adjacent to the mass through the opposing wall frequently reveals the mouth of the diverticulum which establishes the diagnosis. In many of the cases the reaction is not so extensive and the acutely inflamed diverticulum is easily recognized. However, even in the simple acutely inflamed diverticula there is usually an associated indurated inflammatory reaction in the adjacent cecal wall. This makes the excision of these lesions difficult and the closure of the defect very difficult and usually insecure. The technical difficulty encountered in removing these lesions and obtaining a secure closure together with the definite tendency for them to drain into the bowel and subside makes us feel that surgical removal either by the radical procedure or by local excision is definitely contraindicated in most cases.

CONCLUSIONS

1. Acute diverticulitis of the cecum is a condition which cannot be differentiated clinically from acute appendicitis and as a result must occasionally be coped with when operating for acute appendicitis.
2. In the majority of cases, symptoms developed in the patients, under 40 years of age.
3. Diverticula of the cecum are characteristically solitary diverticula and are of the true type.
4. When acutely inflamed they show varying degrees of reaction from a simple acutely inflamed cecal out-pouching to the development of a large indurated inflammatory cecal and pericecal mass.
5. Acute diverticulitis of the cecum should be considered in any patient with acute right lower quadrant symptoms and signs, who previously has had an appendectomy.
6. If a clinical diagnosis of the condition can be made conservative, treatment along with chemotherapy should be instituted.
7. A radical excision of the mass by resection and anastomosis is definitely not indicated. A local excision and closure of the defect in most cases is probably not advisable. Except in those cases which have developed an abscess and in which drainage is indicated, the abdomen should be closed without doing an appendectomy and without drainage, and chemotherapy should be instituted. This is particularly true when an open mouth to the diverticulum can be palpated.

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SYNOVIAL SARCOMA WITH REPORT OF TWO CASES

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HISTORICAL

THE subject of synovial sarcoma abounds in discrepancies and presents a great deal of confusion, particularly when reviewing the literature pertaining to this group of tumors. For example, in reading the bibliographies accompanying monographs dealing with synovial sarcomas, one is struck with the varying histologic standards employed in tabulating the reported cases. As far back as 1894, Salter and Hardie reported a case of primary sarcoma of the synovial membrane of the knee joint in a 25-year-old male patient, and designated the tumor a spindle-cell sarcoma. Yet, this case is rarely referred to in the more recent bibliographies dealing with this subject. The same holds true in the case of Lockwood reported in the Transactions of the London Surgical Society in 1902 under the histologic diagnosis of spindle-cell sarcoma, and the one by Turner in the same year which was designated mixed-cell sarcoma involving the synovial membrane of the ankle joint.

As one commences a review of this group of malignant tumors involving the extremities, one is at first startled to learn what an exceedingly small percentage of cases it comprises. Yet, a more careful study of the literature leads one to suspect that the paucity of available case reports is more apparent than real.

To explain this discrepancy, one must remember that synovial membranes of joints, bursae and tendons consist of a lining stratum composed of specialized connective tissue cells and an underlying layer of fibrocytes. It is quite possible that the variation in histologic features presented may, in a great measure, be due to the point of origin of the tumor in the synovial membrane. Thus, a tumor arising directly from the lining stratum will present the characteristic features of clefts lined with characteristic polyhedral cells, which have been so ably described by Knox, Berger, and DeSanto and associates. On the other hand, a tumor arising from the deep fibrocytic layer will probably present spindle cell characteristics, thereby accounting for the designation of spindle-cell sarcoma of synovial membrane. Another possible explanation of the divergence of designations attributed to these tumors as a result of varying histologic features may be that, as a result of metaplastic changes occurring in the tumor cells by virtue of their location in joints, bursae and tendon sheaths, the cells may take on forms somewhat different from those originally presented, and thus give rise to the variation in nomenclature. Whatever the case may be, it appears

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that the disease is far more prevalent than one is led to believe by a casual survey of the existing literature.

The earliest reported case of synovial sarcoma, according to Knox, was that of v. Ruediger Rydygier in 1906, which concerned a tumor involving the knee joint in a 20-year-old girl. A personal survey of the literature, however, disclosed the fact that as far back as 1894, Salter and Hardie reported a case of spindle-cell sarcoma of the synovial membrane of the left knee joint in a 25-year-old male patient. Antedating the report of Rydygier by four years are two case reports, one by Lockwood, which he designated spindle-cell sarcoma, involving the synovia of the right knee, and the other by Turner called mixed-cell sarcoma of the synovia of the ankle joint. In 1910, Lejars and Rubens-Duval presented the first real compilation of cases of synovial tumors. Because of the perivascular grouping of cells, Faccini, in 1923, reported a case and employed the term sarcomatous perithelioma to describe the tumor. The designation synovioma was given to this group of tumors by Smith, in 1927.

In 1931, Dietz reviewed the literature which comprised ten cases, and added one of his own. The first reported case of synovial sarcoma to appear in the American literature was one reported by Wagner in 1930.

A comprehensive treatise dealing with pathologic entities involving the joints was presented by Sabrazes and his associates in 1932, in which the subject of synovial sarcoma was thoroughly and adequately discussed. In 1936, Knox reviewed the literature and added three cases of her own. Her discussion of the histopathology of the disease was instrumental in placing this group of tumors upon a sounder and firmer pathologic basis than heretofore.

Coley and Pierson, in 1937, reported a group of fifteen cases of synovioma collected from the records of the Memorial Hospital. One year later, Berger reported five additional cases and critically analyzed the existing literature and pointed out that several of the cases reported as synovial sarcomas such as those of Ruediger Rydygier, Hannemuller, the third case reported by Knox, the cases of Faccini, Tavernier, Hodgson and Bishop, and Fievez were really doubtful in that they failed to meet his critical requirements.

ETIOLOGY

Out of a total of 76 collected cases, including the two here reported, a history of trauma was definitely present in 19, an incidence of 25 per cent, too small to signify a causal relationship. DeSanto and associates believe that a large number of these tumors occur in and around the knee joint, thereby suggesting a possible relationship between chronic bursitis and synovitis and synovial sarcoma. The incidence of tumors involving the knee joint and its surroundings as tabulated in this series is 48.7 per cent.

Sex plays an insignificant role in this disease. There were 42 cases among men as against 33 in women. In one instance the sex was not mentioned.

Of the 74 cases where the age was mentioned, 46 patients were between 20 and 40 years of age, an incidence of 62.1 per cent. Beyond 40 there were 21 patients (28.4 per cent), and 7 patients were under 20 (9.5 per cent). The oldest reported case was that of a woman 75 years of age, while the youngest was an infant 9 months old. The average age incidence in the entire group was slightly over 33 years, which is distinctly less than one sees in the group of sarcomas involving fascia and bone.

The most recent monograph fully dealing with this subject was by DeSanto and his associates, in 1941, in which 16 personally observed cases were reported. Snyder reported a case of synovioma of the knee joint in a woman, in 1942, and Briggs presented 9 additional cases in 1942.

PATHOLOGY

Synovial sarcomas originate primarily in synovial tissue, and for this reason are found in joints, bursae and tendon sheaths. In view of the fact that the synovial lining of bursae situated around joints is frequently in direct communication with the synovia lining the adjacent part, it is at times impossible to state with certainty whether a synovial sarcoma situated in the vicinity of a joint has had its origin within the joint or in the bursa adjoining the joint, making tabulation on the question of location somewhat uncertain.

Synovial tumors may be classified as circumscribed, diffuse, and encapsulated. Circumscribed tumors are frequently found in tendon sheaths and bursae. The diffuse variety usually occurs in and around the knee joint and involves the popliteal space and the region above the patella. Encapsulated tumors are usually situated within para-articular bursae.

In general, it may be stated that on gross appearance these tumors are soft and myxomatous, although it is not unusual to find some which are firm and tough. Areas of brownish pigmentation scattered throughout the growth, due to the presence of old blood, are frequently seen. One may also find islands of calcification, bone, and cartilage within tumors.

HISTOPATHOLOGY

The histologic identification of synovial sarcomas is far more difficult than the recognition of other types of sarcomas, and to be conclusive, multiple sections are frequently required. A characteristic feature of such tumors is the presence of spaces or clefts which occasionally contain mucin or blood. The clefts are lined by strands of tissue composed of polyhedral or cuboidal cells often resembling pavement epithelium. Interspersed among these cells one sees areas composed of

closely packed flat and spindle-shaped cells. Both types of cells usually show mitotic figures. The histiocytic features of these tumors are manifested in a variety of characteristic manners. The cells may have large single round or ovoid nuclei and heavy reticulated cytoplasm arranged in strands with little or no evidence of clefts. On the other hand, the cells may be multinucleated, giving the impression of giant-cell sarcomas. Because of the presence of large xanthoma cells in some synovial sarcomas, these tumors may be mistaken for benign giant-cell xanthomas. Unless specimens are taken from various parts of the growth, a section may be obtained with cellular architecture indistinguishable from neuro- or fibrosarcoma. The presence of calcium, bone, and cartilage has been reported in synovial sarcomas. Knox points out that one of the characteristic features of this type of tumor is the presence of swollen cells which result from mucoid degeneration. True mucus has never been found in these tumors.

SYMPTOMATOLOGY

Pain was present in 40 of the 76 reported cases, an incidence of 52.6 per cent. It was a prominent symptom in cases where the tumor involved the knee joint, but was either absent or insignificant in the encapsulated or circumscribed variety.

A tumor was noted in 71 of the 76 cases (93.4 per cent), and was present for an average duration of 30 months. Where the tumor occupied a superficial position as the cubital fossa, olecranon region, or wrist, it was discovered early, while tumors within the confines of the knee joint, or deeply imbedded in the popliteal space, escaped detection until well advanced. The average duration of symptoms was 36 months, ranging from 1 month up to 10 years.

A survey of the 76 collected cases, including the two about to be reported, reveals the fact that the tumor involved the knee joint, including the popliteal space, in 37 patients (48.7 per cent). The elbow joint, including the antecubital fossa, was involved in 8 instances (10.5 per cent), the ankle joint in 7 (9.2 per cent), the foot in 6 (8 per cent), the thigh in 5 (6.6 per cent), and the palm of the hand 3 times (4 per cent). The wrist joint was involved twice (2.6 per cent) as were the fingers also. The space above Poupart's ligament, axilla, forearm tendon sheath, flexor brevis tendon, dorsum of hand and toe were each involved once (1.3 per cent).

PROGNOSIS

For general purposes it may be stated that all synovial sarcomas are malignant to a greater or lesser degree. Those tumors presenting a greater number of multinucleated giant cells are believed to possess less malignant tendencies, yet out of 4 such cases described by DeSanto and his co-workers, 2 promptly recurred after extirpation. One of these has been reported well after 3 years, following 2 local resections.

The most malignant type consists of tumors characterized by closely approximated cells presenting oval or round nuclei. Such tumors, following removal, quickly metastasize to the lungs and bones. Tumors presenting well-defined clefts and cells resembling most the characteristics of synovial cells occupy a position between the two extremes above noted. Knox estimated the interval between the time the patients were first observed and the time of their terminal illness as varying between 7 months and 7½ years.

A survey of the reported cases shows that in the majority of instances, treatment was promptly followed by recurrence and metastases (56.6 per cent). In 13 cases reported by DeSanto and associates, in which local excision was carried out, prompt recurrence took place in 10 of them within 9 months, one patient developed axillary metastases, and the remaining 2 were reported well after 9 and 14 months, respectively.

These same authors reported 7 cases treated by delayed amputation, of which 6 sarcomas were in the knee joint and 1 in the flexor tendon of the ring finger. Only 2 patients, of this group survived, 1 being alive after 22 months, and the other after 1 year.

They recommend wide local excision for the encapsulated and accessible tumors, reserving radical amputation for those tumors which, on histologic study, show a high degree of malignancy, and in cases where local recurrence follows resection. Radical amputation is immediately indicated in all diffuse and inaccessible tumors. Deep roentgen therapy may be of some use as an adjuvant to surgery.

CASE REPORTS

CASE 1.—B. M., aged 30 years, a porter and single, was first seen by us on Oct. 5, 1940, complaining of a small swelling on the palm of the right hand of three years' duration. The family and past histories were negative. He had never had a venereal disease. On close questioning, he thought that he might have traumatized his hand in carrying luggage. Nine months previously a physician had incised this swelling. There was no loss of weight, nor any other symptoms, save for a tendency to tire easily on exertion. The wound did not feel tender, nor give rise to pain.

Physical examination, save for the lesion on the palm of the right hand, was essentially negative. Examination of the right palm disclosed a deep linear wound along the thenar palmar fold, in the proximal end of which there was a shallow opening with a necrotic base which bled easily on palpation. A probe could not be introduced into the deep tissues. Lymphadenopathy was absent at this time.

Roentgenologic examination of the lungs revealed no evidence of metastases. Hemoglobin was 89 per cent.

Superficial x-ray exposures to the right palm were given during the next 3 months. In spite of local dressings with sulfanilamide powder alternating with urea crystals, improvement was not noted. At this time examination disclosed a palpable epitrochlear node in the right arm. The local lesion could best be described as a deep jagged wound extending into the thenar crease of the right palm with a necrotic grayish base. Biopsy revealed the presence of synovial sarcoma.

On Feb. 14, 1941, extirpation of the growth was carried out under cyclopropane anesthesia.

Pathologic Report (Dr. Arthur Schifrin).—The specimen consists of several fragments of tissue removed from different parts of the palm, received fixed in formalin.

Microscopic: (1) Sections from deep palmar fascia area: The fragments are infiltrated by tumor tissue. In some areas the latter form the lining of small cleftlike spaces. This lining is of irregular thickness and in some sites forms small moundlike eminences which project into the lumina of the cleftlike spaces. The cells vary in size and shape. Those closest to the lumen are often larger, more polygonal, and with better defined cell outlines. Their cytoplasm is pale and nuclei are of moderate size, elliptical or round. Some of the nuclei are larger and somewhat lobulated, while others show atypism. Rare ones show mitoses. These cell layers are intermingled with and in continuity with cells which are more numerous in the deeper portions and are definitely smaller, flatter, more spindle shaped, and more closely knitted together. They fuse with the subjacent collagenous connective tissue so that no basement membrane to this entire lining layer can be demonstrated. Scattered and dense collections of round cells are present in the deeper and adjacent portions. The tumor infiltration extends into adjacent fibrous and fatty tissue.

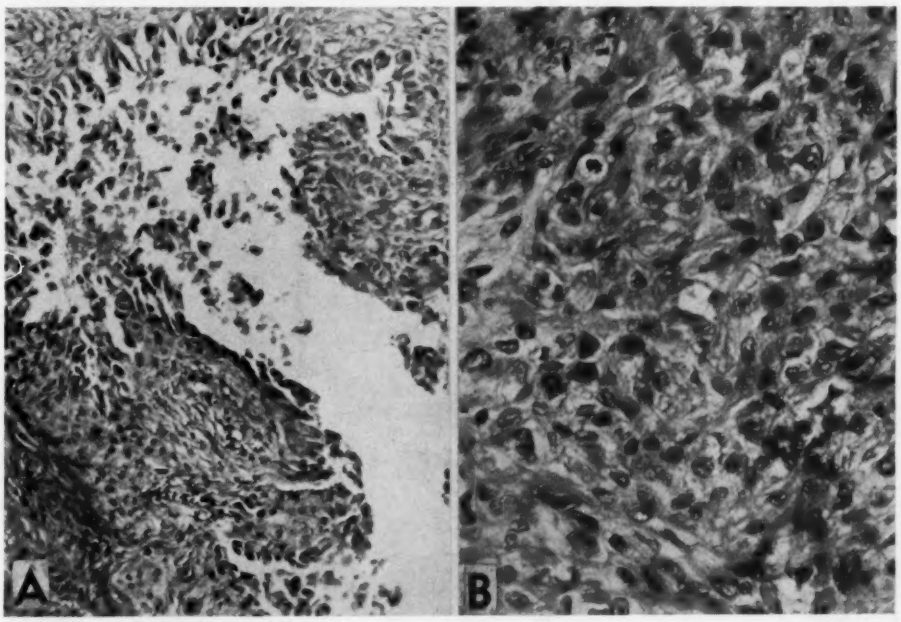

Fig. 1 (Case 1).—*A*, Low-power view showing cleftlike space, lined by imbricated epithelial-like cells. *B*, High-power view showing polygonal, globoid, and pale cells in continuity with spindle-shaped cells; several mitoses and atypical nuclei are seen.

(2) Sections were also taken from nerves, lumbrical muscles, and skin at the resected edge of the operative area. No infiltration was present. Sections taken through the main mass leading down to the deep palmar fascia area showed cleftlike spaces lined by polygonal epithelial-like cells as already described. The skin adjacent to the mass showed tumor infiltration.

Diagnosis: The diagnosis was synovial sarcoma showing infiltration of subcutaneous tissue, fibrous tissue, and fat. The nerve and deeper muscle tissues are not infiltrated.

Radical amputation was refused. Up to the present there has been no recurrence, and the patient is apparently well.

CASE 2.—A. M., a 47-year-old married woman, an artist, was first seen on April 11, 1940, complaining of a painless swelling of the right knee of 10 days' duration, swelling of the ankles, and occasional swelling of the eyelids. There was no history of trauma.

Physical examination was essentially negative. No abnormality was noted around the knee joint.

She was again seen on Oct. 7, 1940, complaining of puffiness around both knees, more marked around the right. At this time examination disclosed a fluctuant swelling on the inner aspect of the right knee which was aspirated, yielding about 30 c.c. of bloodstained fluid. Specimens of the fluid were sent to the laboratory for culture and for microscopic examination of centrifuged sediment for cells. These were reported negative. From that time to Dec. 12, 1940, aspirations were carried out on several occasions, and amounts of fluid varying from 9 to 50 c.c. were removed. X-ray taken on Dec. 19, 1940, failed to show any involvement of bone. On Jan. 13, 1941, 95 c.c. of fluid were aspirated from the right knee, and 2 c.c. of quinine and urethane were injected, and after 5 injections at weekly intervals, the knee appeared normal. Following an examination on April 3, 1941, the patient went on vacation and returned November 13, complaining of swelling and soreness around the right knee. X-ray examination at this time revealed a fusiform elastic swelling arising from the soft parts of the inner aspect of the right knee above the inner condyle of the femur.

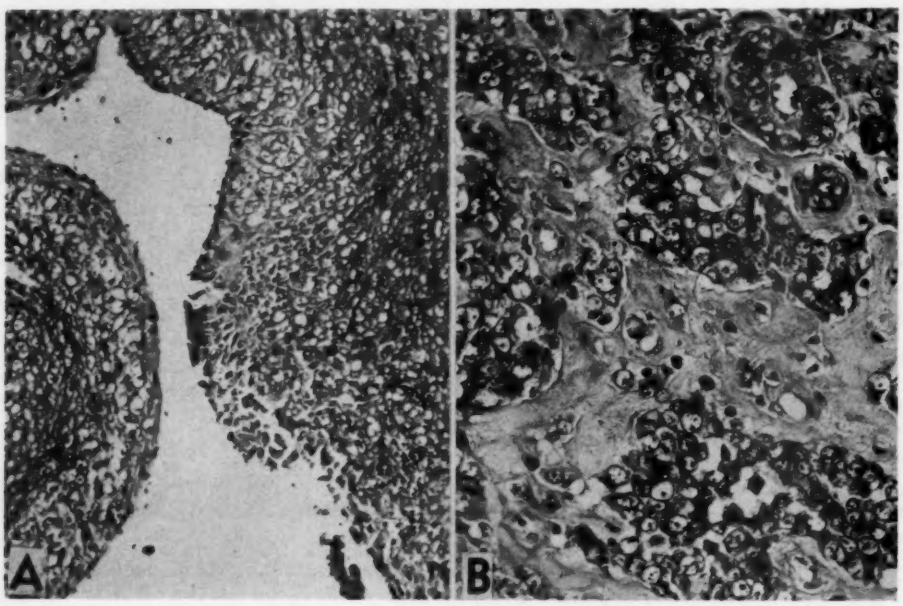

Fig. 2 (Case 2).—*A*, Low-power view showing cleftlike space lined by a broad zone of cellular tissue whose outermost layer contains epithelial-like, pale, polygonal, and globular imbricated cells. *B*, Higher power showing nests of solid syncytial and polygonal cells with regular and atypical nuclei; mitoses are present.

Operation was performed Dec. 11, 1941. Situated beneath the lower fibers of the vastus internus muscle of the thigh, just below the inner aspect of the knee, there was a tumor about the size of a small peach, containing considerable old blood and necrotic tissue. This very closely resembled necrotic papillomatous tissue so frequently found in cases of papillary carcinoma of the bladder. The capsule of the tumor was thickened and adherent to the muscle fibers of the vastus internus.

Radical local excision of this mass was carried out and the wound healed by primary union in 6 days. Three weeks later another and wider dissection was carried out at the Memorial Hospital, followed by deep x-ray treatments. The patient refused amputation. At present she is confined to the hospital with diffuse metastases to the abdomen and lymph nodes.

Pathologic Report (Dr. Arthur Schifrin).—

Macroscopic.—The specimen consists of numerous fragments of tissue. Many portions consist of fibrotic friable tissue. Several broad fragments show a delimiting outer fibrotic wall with no penetration by its contents. The internal surface of these fragments is irregular, rough, shaggy, and friable, and contains papillary elevations of hemorrhagic material which in some places is canary yellow and in other places brownish in color.

Microscopic: The wall of the main lumen is irregular and numerous irregular polypoid elevations project from it. These elevations consist of tumor tissue infiltrating the wall. The tumor tissue includes very cellular areas which contain large cells varying from polygonal cells to cells with large protoplasmic processes and syncytial cytoplasm. The nuclei vary from regular large vesicular nuclei containing distinct nucleoli, to small dark and dense, and often large irregular, bizarre atypical nuclei. Multinucleated cells are present and both regular and irregular types of mitoses are present.

Where the tumor tissue borders a lumen or a cleft, the outermost zone shows a multicellular layer of paler, more succulent cells having a membranous-like appearance. This is in direct continuity with subjacent cells which have a more fibroblastic appearance. Within the cellular areas there are areas of necrosis, interstitial hemorrhage, numerous xanthoma cells, and hemosiderin laden cells. The cytoplasm of the membranous-like portion varies from eosinophylic and granular to pale and clear.

At one site a blood vessel within the capsule shows subintimal tumor-cell infiltration. Where the tissue is quite cellular there are lumina which are possibly artefacts, but there are definite cleftlike lumina which are obviously not artefacts.

Diagnosis: Synovial sarcoma with marked infiltration of the bursal wall.

SUMMARY AND CONCLUSIONS

Synovial sarcoma is a highly malignant tumor arising from synovial membranes of joints, bursae and tendon sheaths. The paucity of case reports of tumors of this type is more apparent than real because of the variance in designations under which they have been recorded. This discrepancy in designation is due to the variation in histologic architecture of the tumor, depending upon the site or origin of the tumor from the various layers of the synovial membrane. Thus, a tumor originating from the lining stratum of the synovial membrane will present certain characteristic features, while one arising from the deep fibrocytic layer will present features closely simulating the ordinary spindle-cell sarcoma. Furthermore, variations in nomenclature may also occur as a result of metaplastic changes occurring in the tumor cells by virtue of their location. Although some tumors are firm and tough, the majority are soft and myxomatous. A characteristic feature of synovial sarcoma is the presence of clefts lined by strands of polyhedral or cuboidal cells resembling pavement epithelium. Areas composed of closely packed, flat or spindle-shaped cells are often interspersed among these strands of cuboidal cells. Large xanthoma

TABLE I

REPORTED CASES OF SYNOVIAL SARCOMA

AUTHOR	AGE (YEARS)	SEX	LOCATION	HISTORY OF PRE-EXISTING TRAUMA OR INFECTION	OUTSTANDING SYMPTOMS			PRE-OPERATIVE DIAGNOSIS	TREATMENT	END RESULTS
					PAIN	TUMOR OR SWELLING	DURATION			
Salter and Hardie, 1894	25	Male	Knee joint	Not given	Positive	Positive	5 yr.	Spindle-cell sarcoma	Local excision followed by amputation	Well 6 mo. later
Lockwood, 1902	24	Female	Knee	None	Positive	Positive	3 yr.	Spindle-cell sarcoma	Local excision	Died 11 hr. after operation
Turner, 1902	28	Male	Ankle	Knocked foot against brass rail	Positive	Positive	2 mo.	Mixed-cell sarcoma	Local excision	Not given
v. Ruediger Rydygier, 1906	20	Female	Left knee	Not given	None	Positive	?	?	Resection of joint tumor	Patient reported well after 11 mo.
Hannemuller, 1909	44	Male	Ankle joint	Not given	Not given	Not given	Not given	Sarcoma	Biopsy followed by local extirpation	?
Lejars and Rubens-Duval, 1910	22	Male	Left knee	None	Positive	Positive	3 yr.	Rheumatism	Removal of tumor from intra-articular surface, followed by amputation	Not given
Chenot and Tzanck, 1912	38	Female	Left astragaloscaphoid joint	None	Positive	Positive	8 mo.	None	Local extirpation	Not given
Faccini, 1923	38	Male	Knee	Not given	Not given	Not given	Not given	Not given	Not given	Not given
Smith, 1927	?	?	Inner aspect of thigh near Hunter's canal	Not given	Not given	Not given	Not given	Not given	Operation (type not given)	Died 6 mo. after operation of pulmonary metastases

Idem	24	Female	Space above Poupart's ligament	Not given	Positive	Positive	8 mo.	Not given	X-ray	Died with metastases
Idem	35	Male	Knee	Not given	None	Positive	5 mo.	Not given	Local excision followed by delayed amputation	Metastases
Wegelin, 1928	28	Male	Outside of left patella	None	None	Positive	?	Not given	Excision	Patient well 5 mo. later
Tavernier, 1930	23	Female	Knee	Not given	Positive	Positive	Several yr.	Periostitis	Excision followed by recurrence and a secondary resection of knee joint	?
Prym, 1930	66	Female	Knee	Not given	?	Positive	7 yr.	Tuberculous arthritis	Local operations followed by amputation	Died in 1 yr. after amputation
Dietz, 1931	Not given	Female	Knee	Injury 5 years previously	?	Positive	5 yr.	Not given	Local removal	Not given
Sabrazes et. al., 1932	18	Female	Left knee	Not given	Positive	Positive	5 yr.	Popliteal cyst or abscess, then tuberculosis	Local excision followed later by amputation	Died 10 yr. after onset of symptoms and 8 mo. after amputation with pulmonary metastases
Cooperman, 1932	21	Female	Flexor brevis tendon	Patient had fallen from a ladder	?	Positive	Not given	Not given	Local excision	Well 8 mo. later
Bonne and Collet, 1935	25	Female	Outside knee joint	Not given	Not given	Not given	Not given	Not given	Not given	Not given
Hodgson and Bishop, 1935	28	Male	Knee joint	Injury to knee 1 year previously	Positive	Positive	7 yr.	Not given	X-ray as prescribed	Death in 1 yr. with metastases in skin and thigh 7 mo. after onset

TABLE I—CONT'D

AUTHOR	AGE (YEARS)	SEX	LOCATION	HISTORY OF PRE-EXISTING TRAUMA OR INFECTION	OUTSTANDING SYMPTOMS			PRE-OPERATIVE DIAGNOSIS	TREATMENT	END RESULTS
					PAIN	TUMOR OR SWELLING	DURATION			
Zwahlen, 1935	22	Female	Forearm tendon sheath	None	Positive	Positive	Several yr.	Tuberculous synovitis	X-ray as prescribed, biopsy followed by amputation	Death 8 yr. after onset of symptoms and 2 yr. after amputation
Idem	16	Male	External malleolus	None	None	Positive	?	?	Local excision followed in 4 years by amputation	Died 3 mo. after amputation with pulmonary and pleural metastases
Fievez, 1935	59	Female	Left ankle joint	Injury 7 years previously	Positive	Positive	7 yr.	?	Amputation 10 years after tumor appeared	Not recorded
Knox, 1936	22	Female	Elbow	None	Positive	Positive	3 yr.	Spindle-cell sarcoma	Local removal 18 months after tumor appeared, followed by amputation	Died 10 yr. after first symptoms, pleural and pulmonary metastases
Idem	33	Male	Popliteal space	None	Positive	Positive	6 mo.	Not given	Amputation	Died of pulmonary metastases about 2 yr. after amputation
Idem	24	Male	Foot	Struck foot 2½ years previously	Positive	Positive	2½ yr.	Hemangioma or sarcoma	Local excision followed by amputation	4 yr. after amputation patient had pulmonary metastases
Black, 1936	36	Male	Palmar aspect of web of thumb	Crushing injury to soft tissues between thumb and forefinger 3 years previously	None	Positive	3 yr.	Not given	Local excision	No recurrence after 6 mo.; believes this tumor benign

Berger, 1938	30	Male	Thigh	None	None	Positive	?	Not given	Local excision	Recurrence after 5 mo.
Idem	38	Male	Thigh	None given	None	Positive	6 mo.	Not given	Local excision	Recurrence with inguinal, abdominal, and pulmonary metastases, and death in 5 mo.
Idem	26	Male	Axilla	None given	None	Positive	3 mo.	Lymphosarcoma	Local excision	Died 2 yr. after onset of tumor with most likely pulmonary metastases
Idem	75	Female	Wrist, adherent to tendon sheath	None given	None	Positive	7 yr.	Not given	Local excision with recurrence in 3 weeks; amputation 7 months later	Not given
Idem	50	Male	Thigh	None given	None	Positive	1 yr.	Not given	Local removal	No follow-up (considered by Berger as a malignant xanthomatous giant-cell tumor)
Brunner, 1936	47	Male	Bursa bicipital space	None given	?	Positive	7 yr.	Adamantinoma	Local removal followed by metastases in 2 months; then local removal and x-ray as prescribed	Axillary recurrence 6 mo. after second removal; death with cerebral metastases 10 yr. after onset
Sabrazes et. al., 1932	50	Male	Elbow	None given	?	Positive	5 yr.	Malignant synovialoma	Local removal	Died shortly after, probably from pulmonary metastases
Coley and Pierson, 1937	45	Male	Index finger	Continual injury of finger in course of work as cabinet maker	None	Positive	7 mo.	Not given	Excision followed by recurrence, followed by x-ray as prescribed	Tumor continues to grow; no further information

TABLE I—CONT'D

AUTHOR	AGE (YEARS)	SEX	LOCATION	HISTORY OF PRE-EXISTING TRAUMA OR INFECTION	OUTSTANDING SYMPTOMS			PRE-OPERATIVE DIAGNOSIS	TREATMENT	END RESULTS
					PAIN	TUMOR OR SWELLING	DURATION			
Idem	9 months	Male	Knee	Not given	None	Positive	7 mo.	Not given	Excision followed by recurrence, then x-ray as prescribed	No recurrence after 3½ yr.
Idem	24	Male	Foot	Not given	Positive	Positive	10 mo.	Not given	Local excision followed by recurrence	Died of pulmonary metastases 2½ yr. after onset of symptoms
Idem	34	Male	Plantar aspect of foot	Not given	Positive	Positive	3 yr.	Not given	X-ray as prescribed followed by amputation	Died of pulmonary metastases 4 yr. after onset of symptoms
Idem	22	Female	Dorsum of hand	Trauma to hand 7 years previously	None	Positive	7 yr.	Not given	Local excision followed by recurrence, then amputation	Died of pulmonary metastases 4 yr. after onset of symptoms and 15 mo. after amputation
Idem	47	Male	Knee	Trauma to knee 4 months before tumor appeared	Positive	Positive	2 yr.	None given	Excision followed by x-ray as prescribed, and then amputation	Died of pulmonary metastases 3 yr. after onset of symptoms
Idem	35	Female	Knee	Trauma 8 years previously	Positive	Positive	8 yr.	None given	Local excision followed by x-ray	Well 2 yr. later
Idem	12	Female	Knee	Not given	Positive	Positive	1 yr.	None given	Local excision followed by x-ray and amputation	Well 6 yr. after operation
Idem	64	Male	Foot	Not given	Not given	Positive	5 mo.	Not given	Local excision followed by amputation	Well 3½ yr. later

Idem	27	Male	Palm	Injury of right palm, with laceration 9 months previously	Positive	Positive	9 mo.	Not given	Excision followed by recurrence, then x-ray as prescribed	Tumor still present 16 mo. later
Idem	16	Female	Knee	None	Positive	Positive	6 mo.	Not given	Local excision followed by recurrence, followed by wide excision, and removal of patella plus x-ray as prescribed	Apparently well 28 mo. after prescribed x-ray
Idem	45	Female	Large toe	None	Positive	Positive	1 mo.	Not given	Excision followed by recurrence and further excision plus x-ray as prescribed	Well 5½ yr. later
Idem	45	Male	Knee	None	None	Positive	3 yr.	Not given	Excision followed by recurrence	1 year later recurrence; amputation advised
Idem	29	Female	Popliteal space	None	Positive	Positive	9 yr.	Not given	Local excision followed by recurrence and excision	Died of pulmonary metastases 9 yr. after onset of symptoms
Idem	44	Female	Dorsum of foot	None	None	Positive	1 yr.	Not given	X-ray as prescribed	No change in patient's condition
DeSanto et al., 1941	30	Male	Antecubital fossa	Not given	None	Positive	6 mo.	Fibrosarcoma	Local excision plus x-ray as prescribed	Alive with axillary metastases after 14 mo.
Idem	63	Male	Elbow	Not given	None	Positive	2 yr.	Not given	Local excision	Alive and apparently well after 11 mo.
Idem	50	Female	Elbow (olecranon bursa)	Not given	Positive	Positive	10 yr.	Olecranon bursitis	Local excision; refused amputation; recurrence	Recurrence 6 mo.

TABLE I—CONT'D

AUTHOR	AGE (YEARS)	SEX	LOCATION	HISTORY OF PRE-EXISTING TRAUMA OR INFECTION	OUTSTANDING SYMPTOMS			PRE-OPERATIVE DIAGNOSIS	TREATMENT	END RESULTS
					PAIN	TUMOR OR SWELLING	DURATION			
Idem	26	Female	Thigh	Not given	Positive	Positive	9 mo.	Not given	Local excision, x-ray as prescribed; recurrence	No further data
Idem	23	Male	Knee joint	Hit knee joint shortly before onset of symptoms	Positive	Positive	18 mo.	Chronic traumatic synovitis	Amputation plus Coley's serum	Died 13 mo. after amputation with pulmonary metastases
Idem	22	Male	Knee (bursa?)	Spiked on lateral aspect of knee 3 years previously	Positive	Positive	3 yr.	Not given	Local excision followed by recurrence in 3 months, and than excision; refused amputation	No recurrence after 1 yr.
Idem	37	Female	Knee joint	Wrenched knee 2½ years previously	Positive	None	2½ yr.	Internal derangement of knee joint	Amputation	Alive with pulmonary metastases after 2½ yr.
Idem	24	Male	Knee joint	Injury of knee after falling down a flight of stairs	Positive	Positive	6 yr.	Calcified popliteal cyst	Local excision, deep x-ray, and delayed amputation	Died of pulmonary metastases 2½ yr. after amputation
Idem	34	Female	Wrist region	None	None	Positive	6 yr.	Not given	Local excision	No recurrence in 9 mo.
Idem	25	Male	Knee joint	?	Positive	Positive	6 to 8 yr.	Traumatic arthritis and possible ruptured meniscus	2 local excisions and delayed amputation	Died of pulmonary metastases 10 mo. after amputation

Idem	32	Female	Flexor tendon of ring finger	None	Positive	Positive	Few mo.	Dupuytren's contracture	Local excision, deep x-ray as prescribed and radium, followed by delayed amputation	Well 19 mo. after amputation
Idem	48	Male	Popliteal space	None	None	Positive	1 mo.	Not given	2 local excisions	Well 2 yr. later
Idem	46	Male	Popliteal space	None	Positive	Positive	1 mo.	Cyst of popliteal space	Local excision, synoviectomy, and amputation	Well 1 yr. after amputation
Idem	45	Male	Antecubital fossa	None	Positive	Positive	40 da.	Not given	Local excision plus x-ray as prescribed	Died of generalized metastases in 7 mo.
Idem	40	Male	Knee	None	None	Positive	2 yr.	Fibrosarcoma	Excision and x-ray as prescribed	Died of pulmonary metastases in 18 mo.
Wagner, 1930	35	Male	Knee joint	None	None	Positive	10 yr.	Chronic synovitis	Repeated local excisions, deep x-ray as prescribed and delayed amputation	Died of pulmonary metastases 10 yr. after amputation
Snyder, 1942	35	Female	Left knee	Followed an attack of sinusitis	Positive	Positive	2 yr.	Angioma	Local excision followed by amputation and x-ray as prescribed	Well 18 mo. later
Briggs, 1942	17	Female	Right ankle	Injury to right ankle 4 months previously (mild blow)	None	Positive	4 mo.	Not given	Excision and x-ray as prescribed	Recurrence 1 yr. later with inguinal metastases; death from pulmonary metastases 5 yr. later
Idem	45	Female	Head of left fibula	None	Positive	Positive	4 yr.	Not given	Excision and x-ray as prescribed	Living and well with no recurrence 7 yr. later
Idem	30	Female	Left foot	None	Positive	Positive	2½ yr.	Simple benign cyst	Excision and x-ray as prescribed	Recurrence 2 yr. later, followed by amputation; death from pulmonary metastases 1 yr. after amputation

TABLE I—CONT'D

AUTHOR	AGE (YEARS)	SEX	LOCATION	HISTORY OF PRE-EXISTING TRAUMA OR INFECTION	OUTSTANDING SYMPTOMS			PRE-OPERATIVE DIAGNOSIS	TREATMENT	END RESULTS
					PAIN	TUMOR OR SWELLING	DURATION			
Idem	22	Female	Left ankle	Injury by falling and striking left ankle 2½ years previously	None	Positive	2½ yr.	Not given	Excision and x-ray as prescribed	No recurrence 18 mo. following operation
Idem	45	Male	Left knee	None	Positive	Positive	3 yr.	Fascial sarcoma	Mid-thigh amputation	Living and well 4 yr. after operation
Idem	17	Male	Left elbow	None	None	Positive	4 mo.	Benign cyst	Excision and x-ray as prescribed followed by second excision 1 year later	Living and well 7 yr. later
Idem	35	Female	Right knee	Outer surface of right knee struck 7 years previously	Positive	Positive	7 yr.	Not given	Mid-thigh amputation and x-ray as prescribed	Death from pulmonary metastases 4 yr. later
Idem	25	Male	Left popliteal space	None	Positive	Positive	3 mo.	Bursal cyst	Local excision	Recurrence in 4 mo., and death from pulmonary metastases 5 mo. later
Idem	27	Male	Left popliteal space	None	None	Positive	5 wk.	Not given	Excision and x-ray as prescribed	Under treatment for second recurrence
Lazarus and Marks, 1943	30	Male	Palm of hand	?	None	Positive	3 yr.	Synovial sarcoma	Local excision and x-ray as prescribed	Well 14 mo. later
Idem	47	Female	Knee	None	Positive	Positive	15 mo.	Bursitis	Local excision and x-ray as prescribed	Diffuse metastases to abdomen and lymph nodes 13 mo. later

cells are occasionally seen, which may lead to the erroneous diagnosis of benign giant-cell xanthoma. According to Knox, one of the characteristic features of this type of tumor is the presence of swollen cells which result from mucoid degeneration, although mucus has never been found in these tumors.

A careful review of the literature discloses the presence of 76 recorded cases, including two of ours which are presented here. Of this number, there was a history of trauma in 19 (25 per cent). Forty-six of the 76 patients were between the ages of 20 and 40 (62.1 per cent). Pain was present in 52.6 per cent of patients, but when the tumor involved the knee joint it was a prominent symptom. A tumor was noted in 93.4 per cent of cases and was present for an average duration of 30 months. The average duration of symptoms was 36 months. The knee joint was involved in 48.7 per cent of cases, the elbow in 10.5 per cent, and the ankle in 9.2 per cent, while the palm of the hand was involved in only 4 per cent of the cases.

The prognosis is poor. The least malignant tumors are supposedly those containing a greater number of multinucleated cells, while those characterized by closely approximated cells presenting oval or round nuclei display the highest degree of malignancy. Tumors presenting well-defined clefts and cells resembling most the characteristics of synovial cells occupy a position between these two extremes.

A survey of the reported cases shows that in 56.6 per cent prompt recurrence and metastases followed treatment. According to Knox, the interval between the time of onset of symptoms to the time of the terminal illness varied between 7 months and 7½ years. In our tabulated series of 76 cases, there were follow-ups on 64 patients, and of this number, 10 (16 per cent) were found to be living 5 years or more, while 9 (14 per cent) were alive between 3 and 5 years. Eight patients (13 per cent) succumbed between the first and third years, and 15 (24 per cent) died within the first year. Twenty-one persons (33 per cent) were reported well without further comment.

Local wide excision is advocated for the encapsulated and accessible tumors. Radical amputation is reserved for tumors showing, on histologic examination, a high grade of malignancy, or where local recurrence followed extirpation, and also in inaccessible tumors. Irradiation is advocated only as an adjuvant to surgical intervention.

Two cases of synovial sarcoma are here presented, one involving the palm of the hand, and the other the knee joint.

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METASTATIC BRAIN ABSCESS

Complicating Inconspicuous Pulmonary Suppuration in the Presence of Chronic Nontuberculous Empyema

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DURING the years 1934 to 1941, inclusive, 343 cases of nontuberculous empyema have been treated in the University of Michigan Hospital. Of these, 132 were considered chronic. All cases classified as chronic had a known duration of three months or longer. Six of these cases of chronic empyema were complicated by metastatic brain abscesses, an incidence of 4.5 per cent. The diagnosis in each case was confirmed by post-mortem examination. The review of these cases was stimulated by the recent, unexpected death of two patients having chronic empyema, occurring within a three-day period. The cause of death in both patients was a metastatic brain abscess.

This study was begun solely as a review of the cases of chronic nontuberculous empyemas complicated by metastatic cerebral abscesses. A careful study of the post-mortem findings in each revealed that five of the six cases reported harbored a variety of pulmonary lesions beneath the empyema space, each of which was a probable source of septic emboli. In only one case was the pulmonary tissue underlying the pleural space free of suppuration. The significance of these findings became evident when it was found that in four cases no residual empyema space existed at the time of death.

Such metastatic cerebral abscesses follow the occlusion of cerebral vessels by an infected embolus, arising at the site of intrathoracic suppuration and circulating freely in the blood stream (Eagleton). The course of the embolus, from its point of origin to its terminal lodging, has occasioned various theories. Virchow, in 1853, postulated an origin in a small tributary of one of the pulmonary veins, the particle being then transported through the pulmonary veins, the left heart, and the carotid artery and deposited in a terminal radical of a cerebral artery. Eagleton,[3] however, believes that the pathway of the emboli from the chest to the brain is entirely venous and asserts that the rapidity of arterial flow tends to prevent lodgment of an embolus in the arterial circulation. His premise that the emboli pass entirely through veins gains some confirmation in the work of Batson[4] who has demonstrated connections between the intercostal and azygos veins, the paravertebral venous plexus and the cerebral veins. Because of the low pressure within this system and the absence of valves, reversal of flow readily occurs with increase in

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intrathoracic pressure, as in coughing or straining. At least two possible routes are thus open for an infected embolus freed from its empyema source to gain entrance into a cerebral vessel.

CASE REPORTS

CASE 1.—J. G. (No. 368464) was a white man, aged 43 years. The patient was admitted to the Univerity of Michigan Hospital on Sept. 6, 1935, complaining of a productive cough and pain in the right lower chest. The previous history related the onset of acute mid-abdominal pain in 1928, following drainage of a right subdiaphragmatic abscess, in another hospital. A series of bronchoscopic aspirations, before admission to the University Hospital, had given no relief of his presenting pulmonary symptoms.

On admission the scar at the site of the previous subdiaphragmatic drainage appeared well healed. The temperature was 99.5° F. The patient was not acutely ill. Roentgenograms revealed a chronic pneumonitis at the right base with an obliterative pleuritis. After lipiodol bronchograms had been made, a small saccular area, thought to be a small pleural abscess, was noted at the extreme anterior axillary segment of the middle lobe. Thoracentesis revealed pus containing *Streptococcus viridans*. A rib resection was done on September 15, and an empyema cavity was entered. There was a communication with a small subdiaphragmatic abscess, and a fistulous track entered a branch of the middle lobe bronchus. The postoperative course was essentially uneventful. Because of a small, persistently draining sinus, a segment of osteomyelitic rib was removed on October 24. At the time of the patient's discharge from the hospital on November 27, there was a draining sinus at the empyema drainage site which, upon probing, led inward for three inches toward the resected rib. The bronchopleural fistula had closed.

On Jan. 12, 1936, the patient was readmitted because of persistent drainage, apparently due to further osteomyelitic involvement of the sixth rib. Roentgenograms showed an osteomyelitis and an extensive pleuritis at the right base. Further resection of the involved rib was done on January 15, at which time the bronchopleural fistula was again demonstrated. Again the patient's course was uneventful until, on February 13, there was a sudden loss of consciousness with difficult respiration. The attack lasted about one hour. The blood pressure during this period was 90/60. There were no convulsions and no localizing signs during the attack. During the following two days the patient complained of a frontal headache and there was some drowsiness. On February 19, the drowsiness became more marked and the patient became disoriented. At no time were convulsions noted. Neurologic examination revealed slight fullness of the retinal veins without papilledema. The reflexes, both deep and superficial, were normal. Because of the absence of definite localizing signs, craniotomy was not done. The patient died on February 21.

Post-mortem examination revealed a frontal lobe abscess measuring 7 cm. in diameter. Grossly, the adjacent white matter was yellowish green in color and very hyperemic. Microscopically, the brain tissue forming the wall of the abscess was extensively destroyed and was undergoing liquefaction necrosis. There was an associated leptomeningitis at the base of the brain, and particularly in the cisterna magna. The pleural space on the right was obliterated by dense adhesions except at the site of the bronchopleurocutaneous fistula. The underlying pulmonary tissue disclosed a chronic fibroid pneumonia with a chronic purulent bronchitis and bronchiectasis.

CASE 2.—G. W. (No. 402288) was a white man, aged 33 years. The patient was admitted to the University Hospital in coma on May 14, 1937. A scanty history, obtained from his relatives, revealed that an empyema had been drained six years previously. The wound had healed but had required three or four subsequent drain-

ages, each presumably inadequate. There was relief of symptoms after each drainage for a short period of time.

The patient had been in ill health for six weeks prior to admission. Five days before admission he became irrational and in the interim before admission there had been two generalized convulsions. The temperature was 97° F.; the patient was obviously moribund. There was questionable rigidity of the neck. The left thorax showed retraction and limited expansion with the physical signs of a considerable pleural effusion. The blood pressure was 130/64. A small draining sinus was noted in the left mid-axilla; above it, two healed scars were visible. The liver was enlarged. All reflexes were hyperactive and ankle clonus was sustained bilaterally. The patient died eight hours after admission. Roentgenograms were not obtained.

Post-mortem examination revealed a right frontal lobe abscess measuring 4 by 4 cm. It was not walled off from the surrounding brain tissue. The abscess cavity contained heavy green pus under considerable pressure. There was a fibrinopurulent pachymeningitis in the region of the abscess. The chest showed a chronic undrained left empyema, the surrounding pleural wall of which was from 2 to 4 mm. in thickness. The empyema space contained bloodstained purulent material. The draining sinus in the seventh intercostal space entered a small cavity containing necrotic lung, but it did not communicate with the empyema. The underlying pulmonary tissue showed acute passive congestion and edema with a chronic pneumonitis near the hilum.

CASE 3.—R. S. (No. 414883) was a white man, aged 51 years. The patient was admitted to the University Hospital on December 15, 1937. He had been apparently well until October, 1936, when he developed a right "pleural pneumonia," with which he was in bed for three weeks. Following this he was somewhat improved, but continued to have mild symptoms until May, 1937. At this time a right-sided empyema was diagnosed and drained. A drainage tube was left in place for a period of seven months and was removed shortly before admission. The sinus track drained intermittently after removal of the tube. He had recently complained of pain in the right chest, and had developed a cough productive of yellow sputum. Six days before admission there was a sudden onset of generalized tonic convulsions, mostly of the right side, which lasted for one-half hour. There was no loss of consciousness or incontinence. Two more attacks occurred during the evening of the same day and lasted from ten to fifteen minutes each. For the next four days the patient appeared normal. On the day before his admission, there was again loss of consciousness without muscle twitching or incontinence. Following recovery, the patient was drowsy and appeared to have a poor memory. His speech was thick and difficult to understand. On December 15, the day of admission, there were three more attacks, each lasting about thirty minutes, and without vomiting, headache, or incontinence. The temperature was 99.6° F. Examination revealed a complete aphasia and a slight right facial palsy. A complete flaccid paralysis of the right arm and leg was present. There were no signs of increased intracranial pressure. Roentgenograms showed an unresolved pneumonia with a small localized empyema. After admission there was increasing lethargy and a daily temperature elevation to 100° F. Craniotomy was deferred in the hope that the suspected brain abscess would become walled off. Terminally the temperature rose to 103° F. and the patient had marked dyspnea. He died on the fifth hospital day.

At post-mortem examination a brain abscess, measuring 3 by 2.5 cm., occupied the left precentral area. The abscess had ruptured into the left lateral ventricle which contained thick, greenish-gray, foul pus. The path of extension showed very little reaction. In addition, a fibrinopurulent pachymeningitis and leptomeningitis were noted about the left cerebrum and the undersurface of the brain. The right pleural space was almost completely obliterated by dense adhesions below the third rib anteriorly and posteriorly. The pleurae measured 1 cm. in thickness. No free pus

was present. The subjacent lung showed a chronic fibroid pneumonia with organizing fibrin in the alveoli. There were multiple microscopic pulmonary abscesses throughout. The liver contained a chronic abscess cavity measuring 3 cm. in diameter.

CASE 4.—B. F. (No. 420322) was a white boy, aged 4 years. The patient was admitted to the University Hospital on March 26, 1938. In August, 1937, he was seen by his physician because of a stiff neck, pain over the left trapezius muscle, and fever. These symptoms disappeared spontaneously. During the first part of March, 1938, they reappeared, and in addition, a hot, tender swelling appeared over the trapezius.

On admission, the temperature was 99.4° F. There was a 10 cm., indurated, tender, poorly outlined mass over the left trapezius muscle. A left scoliosis was present. Dullness to percussion with diminished breath sounds and fremitus was noted at the left pulmonary apex posteriorly. Roentgenograms of the chest showed obscuration of the left apex, diminished aeration of the left lung, and increased soft tissue shadows in the left cervical and supraclavicular areas with included gas in the tissues. A diagnosis of empyema necessitatis was made, and thoracentesis posteriorly yielded thick, foul, yellow pus which contained *Str. viridans,* fusiform bacilli, and Spirochaetae. Drainage of the empyema through the fourth rib bed posteriorly was carried out on April 4, 1938. At operation the empyema cavity extended from the fourth rib to the apex of the thoracic dome. The postoperative course was uneventful until April 7, when the patient suddenly became unresponsive. No convulsions were noted. Examination at this time revealed left facial weakness, slight weakness of the left arm and leg, papilledema, a positive Kernig's sign, and bilateral sustained ankle clonus with a positive Babinski sign. Lumbar puncture showed increased pressure and a clear fluid which contained thirty cells per cubic millimeter, lymphocytes predominating. The clinical impression was a right cerebral abscess, probably metastatic. A craniotomy was performed on the same day by Dr. Carl F. List, disclosing a nonencapsulated right frontal lobe abscess from which a *Str. viridans* was cultured. After sealing the meninges to the cortex with an electrocautery, the abscess was opened and packed. Sulfonamide therapy was started on the day of operation and was continued until death twenty-three days later.

Post-mortem examination revealed a huge, drained brain abscess replacing the entire right frontal lobe, with extensive surrounding suppurative encephalitis. The purulent process had ruptured into the right lateral ventricle, from which there had been extension into the opposite lateral ventricle and the fourth ventricle. There was a small undrained abscess in the left parietal lobe. A diffuse purulent leptomeningitis was present. Examination of the thorax showed an obliteration of the pleural space over the left apex with a 5 cm. draining sinus posteriorly. No free pus was present. The underlying lung showed an acute purulent bronchitis and a few scattered areas of bronchial pneumonia in the right and left lower lobes.

CASE 5.—H. K. (No. 475011), a white man, aged 35 years, was admitted to the University Hospital on Feb. 3, 1941. He had been referred to the hospital with mild fever, chronic debility, and inadequate drainage of a postpneumonic empyema of three months' duration. Roentgenograms on admission revealed an extensive pyopneumothorax extending from the diaphragm to the thoracic dome on the left side. There was a narrow sinus posteriorly which drained a small amount of thick pus. The sinus track was dilated and a drainage tube of adequate size inserted. Constant negative pressure was maintained in the empyema space by means of a suction apparatus. Re-expansion of the lung almost completely obliterated the empyema space in eight weeks' time. The patient was discharged in good condition with a small tube in the chest wall. He was readmitted on May 9, 1941, with a story of good health until two and one-half weeks previously, when a fall while intoxicated resulted in a contusion of the left supra-orbital area. There was no loss of consciousness at the time. Vertigo, mild nausea, and recurrent right-sided convul-

sions had been present for a week prior to admission. Examination after admission revealed a right hemiplegia with some sensory changes. The small residual empyema was well drained. A craniotomy was performed by Dr. Carl F. List on the day following admission and an unencapsulated brain abscess in the left parasagittal area was drained. *Str. viridans* was cultured from the evacuated pus. The patient received 6 Gm. of sulfathiazole daily from the time of admission. The post-operative course was steadily downhill with increasing coma. Death occurred on May 23.

At post-mortem examination a multiloculated, unencapsulated brain abscess was present in the left parietal area. There were four locules, each measuring at least 2 cm. in diameter and all communicating with each other. There was a diffuse purulent leptomeningitis. No evidence of skull fracture was found. The left pleural space was obliterated by an adhesive pleuritis except for a small sinus track at the site of previous drainage; no free pus was present. The underlying pulmonary tissue showed extensive fibroid pneumonia, bronchiectasis, and a terminal, purulent, lobular pneumonia. Several small hemorrhagic infarcts were noted.

CASE 6.—E. O. (No. 481806), a white man, aged 31 years, was admitted to the University Hospital on May 22, 1941, with a two-day history of staggering gait and repeated left-sided convulsions. In February, 1941, he had had an attack of pneumonia complicated by a right empyema. Following drainage on three occasions he improved, but was still in poor general health, although not confined to bed. On admission, a small draining sinus was noted in the lower right posterior chest. There were physical signs of pleural fluid over the lower half of the right chest posteriorly. The patient was semi-stuperous and had weakness of the left side of the body. The sinus track in the right side of the chest was dilated and a larger tube was inserted, releasing several ounces of thick pus. By probing, the empyema cavity was found to extend to the thoracic dome. Neurosurgical consultation on admission suggested the diagnosis of metastatic brain abscess. Craniotomy by Dr. Ward W. Woods, May 26, revealed an abscess in the right parietal lobe and the abscess was drained through an exploring needle. *Str. viridans* was cultured from the pus. The patient received 6 Gm. of sulfanilamide daily from May 24, until his death on May 27.

Post-mortem examination revealed an unencapsulated right parietal lobe abscess measuring 3 by 1 cm. There was a diffuse purulent leptomeningitis over the right cerebrum. The empyema was dependently and adequately drained. The lung beneath the empyema showed a chronic fibroid pneumonia, bronchiectasis, and an acute purulent and hemorrhagic pneumonia, probably terminal. A thrombus containing many leucocytes was noted in a small pulmonary vein.

DISCUSSION

It has been stated by Evans[1] that it is the tendency of chronic empyemas to form a chronic type of brain abscess, which is generally solitary and almost invariably the only lesion indicative of pyemia. In none of our reported cases, however, was chronicity of the brain abscess a noteworthy factor. Four of our cases showed a duration of from five to ten days from the onset of symptoms to death. The patient with a brain abscess in Case 5 was operated upon eight days after onset; he died thirteen days after operation. In four of the cases the abscess was solitary; in one, multilocular, and in one, multiple.

The cause of death in most reported cases[8] was due to rapid extension of the abscess, with frequent rupture of the abscess into a ventricle. In our third and fourth cases, rupture occurred into the lateral ventricles.

In all the cases, a purulent meningitis was present. In none was true encapsulation present. Kahn[9] is of the opinion that metastatic abscesses, with the exception of those associated with a generalized pyemia, are caused by mixed organisms and do not tend to become encapsulated. In the cases reported in this series, anaerobic cultures of the evacuated pus were not obtained. Grant[2] states that the thorough walling off of a subcortical area of infection within the brain requires about four weeks from the onset of symptoms. In our six cases the duration of symptoms from onset to death ranged from five to twenty-three days.

The ante-mortem diagnosis in each of our cases was a metastatic brain abscess whose site of origin was a chronic empyema. At post-mortem examination, however, the empyema cavity was found completely obliterated in four of the six cases; the pleurae were fused into a thick, heavily scarred layer and only a sinus track in the thoracic wall remained. These findings suggest that pleural infection was quite unlikely as the source of the brain abscess, at least in these four patients. Autopsy did show that bronchiectasis was present in four of the six patients (Case 6 had, in addition, a thrombus in one of the small pulmonary veins) and that multiple, small microscopic pulmonary abscesses were present in the fifth case (Case 3). Only in Case 4 was chronic intrapulmonary suppuration absent; empyema was, therefore, the most likely source of the emboli to the brain only in this patient.

Hedblom[10] reports 310 cases of chronic empyema with one death from a metastatic brain abscess. This is the only published report of the incidence of this complication in a given number of cases of chronic empyema. The status of the lung beneath the empyema pocket was not described.

The reported incidence of empyema in metastatic brain abscess has shown considerable variation in the reports of brain abscess associated with some form of intrathoracic suppuration. In none of the reported figures are the empyemas classified as either acute or chronic and no account is given of the pulmonary tissue adjacent to the empyema space. Schorstein,[7] in 1909, reported 19 cases of metastatic brain abscess from intrathoracic suppuration, of which three are said to have resulted from empyema, an incidence of 15.7 per cent. In 1931, Evans[1] reported 22 cases of brain abscess, five or 22.7 per cent occurring in the presence of empyema. In 1934, Cohen[5] reported 19 cases, four of which also had empyema, an incidence of 21.0 per cent, while Nickerson,[6] in 1935, found only one empyema in 12 cases of brain abscess, an incidence of only 8.3 per cent. The metastatic abscesses not reported as due to empyema were assumed to have arisen from either pulmonary abscess or bronchiectasis which was clinically present in the nonempyema cases. King,[8] in reviewing the reported cases of metastatic brain abscess from empyema or pulmonary suppuration in 1936, found only two patients living following operation for brain abscess that had occurred in the presence of empyema. He assumed that the abscesses were well encapsulated in both cases.

In the above 72 collected cases with metastatic cerebral abscesses quoted from various authors, 82 per cent arose from intrinsic pulmonary suppuration and only 18 per cent, or 13 cases, were attributed to empyema. We are of the opinion that a high percentage of these 13 cases would have shown some degree of suppuration in the adjacent pulmonary tissue if this had been closely examined, and that if such pulmonary suppuration were present it was a more likely source of metastatic brain abscess than the empyema.

SUMMARY

1. During the years 1934 to 1941, inclusive, 343 cases of empyema have been admitted to the University of Michigan Hospital. Of this group, 132 cases were considered chronic. Six of these patients with chronic empyema died of metastatic cerebral abscess, an incidence of 4.5 per cent.

2. The six cases with their autopsy findings are reported in detail. In four of the cases the previous empyema space was obliterated. Five of the six cases displayed varying degrees of chronic parenchymal pulmonary suppuration. This was considered a more probable source of emboli than the pleural infection.

3. Adequate and dependent drainage of the empyema was established in four of the six cases after admission to the hospital. No definite correlation was noted between manipulation at the empyema drainage site and the onset of cerebral symptoms.

4. In four of the reported cases the cerebral abscess was solitary; in one, multiple, and in one, multilocular. In none of the cases has encapsulation of the abscess been present. All had a purulent meningitis and in two cases rupture of the abscess into the adjacent lateral ventricle occurred.

5. In three cases of brain abscess exploratory craniotomy was done; in two of the cases the abscess was drained surgically, while in one the abscess was evacuated through the exploring needle. Appropriate chemotherapy with one of the sulfonamide compounds was carried out in these three cases.

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BLEEDING TIME IN MICE FOLLOWING THE ORAL ADMINISTRATION OF 3,3′-METHYLENE-BIS-(4-HYDROXYCOUMARIN)

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LINK and his associates[1] showed that the hemorrhagic agent in spoiled sweetclover hay prolonged the prothrombin time in animals. Butt and co-workers[2] and Bingham and co-workers,[3] following the administration of the hemorrhagic agent to human beings and dogs, observed prolongation of coagulation and prothrombin times. We found that excessive doses of heparin injected subcutaneously into mice prolonged the coagulation time and in some cases the bleeding time.[4] Therefore, it was of interest to determine if the hemorrhagic agent identified by Stahmann, Huebner, and Link,[5] when administered orally to mice, would affect the bleeding time. The coagulation and prothrombin times were compared with the bleeding time to evaluate better the degree of bleeding tendency produced by this substance.

METHODS

Bleeding times were determined as previously described.[4] Coagulation times were done by the capillary method on blood from the tip of the mouse's tail.

Prothrombin times were performed on oxalated blood drawn from the mouse's heart. No difficulty was encountered with this test. Values will check closely if the following procedure is adhered to for the amount of sodium oxalate used. A 1 c.c. syringe with a 25 gauge needle was rinsed in distilled water. Sodium oxalate was drawn to the 0.2 c.c. mark and then the syringe was emptied. The volume of sodium oxalate which remained in the needle was found to be 0.05 c.c. With this volume of sodium oxalate, 0.2 c.c. of blood was diluted and mixed in the syringe. Prothrombin time studies were done in duplicate tests on 0.1 c.c. of blood placed on dry glass spot plates. A mixture of 0.2 c.c. of equal parts of rabbit brain thromboplastin suspension and $CaCl_2$ solution was added. The prothrombin time was determined by probing the contents on the spot plate with a pointed glass rod. The salt solutions and the thromboplastin used in this study were prepared as described by Quick.[6] Rabbit brain thromboplastin, 100 mg., was suspended in 5 c.c. of 0.9 per cent

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NaCl solution. The thromboplastin suspension was incubated for ten minutes at 50 to 55° C. with intermittent stirring. The supernatant fluid was decanted after standing ten minutes at room temperature and was mixed with an equal volume of $CaCl_2$ solution.

3,3′-Methylene-bis-(4-hydroxycoumarin)* in 0.1 and 0.2 per cent concentrations was suspended in 2 per cent acacia. This suspension was administered orally with a syringe and a blunt 18 gauge needle. The mice received from 10 to 100 mg. per kg. daily for three days and the tests were performed on the fourth day. After the tests were completed the animals were sacrificed and examined grossly for evidence of subcutaneous hemorrhage.

RESULTS

The normal bleeding time varied from 27 to 222 seconds in this group of mice, which was in agreement with previous findings.[4] Coagulation time with the capillary method ranged from 60 to 255 seconds with an average of 153.4 seconds. Prothrombin time in 62 duplicate tests was 15 to 28 seconds with an average of 22.4 seconds. When the bleeding time and the coagulation time were longer than 300 seconds, the values were considered significantly prolonged. Prothrombin time longer than 30 seconds was considered abnormal.

Results on 10 mice which received 4.8 to 6.0 mg. of 3,3′-methylene-bis-(4-hydroxycoumarin) orally per 20 Gm. of mouse weight within a period of 72 hours are tabulated in Table I. The results show normal variation

TABLE I

BLEEDING, COAGULATION, AND PROTHROMBIN TIME IN MICE BEFORE AND AFTER THE ORAL ADMINISTRATION OF 3,3′-METHYLENE-BIS-(4-HYDROXYCOUMARIN) FOR THREE DAYS

MOUSE NUMBER	BLEEDING TIME (SECONDS)	COAGULATION TIME (SECONDS)	PROTHROMBIN TIME (SECONDS)	TOTAL DOSE PER 20 GM. (WEIGHT IN MG.)	BLEEDING TIME (SECONDS)	COAGULATION TIME (SECONDS)	PROTHROMBIN TIME (SECONDS)
11	124	185	26	4.8	120 420	165	28
43	66	130	18	4.8	34 480	158	24
44	75	165	20	4.8	45 300	495	169
2	42	60	21	4.8	190 118	870	109
1	87	85	23	4.8	55 120	1050	148
6	96	195	25	6.0	780	301	47
31	138	180	24	6.0	136 360	1200	>180
35	67	168	24	6.0	>900	1500	>180
26	122	122	21	6.0	105 115	65	26
37	190	178	21	6.0	180 120	93	22

*Supplied kindly by Dr. J. F. Biehn, Abbott Laboratories, North Chicago, Ill.

in bleeding time, coagulation time, and prothrombin time, and the effect of the hemorrhagic agent on these tests. Mice 11 and 43 showed prolonged bleeding time with normal coagulation time and prothrombin time. Usually, we found when one of the tests was normal, the remaining two were also in the normal range as indicated by Mice 26 and 37. However, mice were found in which the prothrombin time and the coagulation time were prolonged while bleeding time was normal (Mice 1 and 2). Most frequently, however, when the bleeding time was prolonged, the coagulation time and the prothrombin time were also increased (Mice 6, 31, 35, and 44). Table I shows that a marked disparity can occur between duplicate bleeding time tests. In some animals a prolonged bleeding time was present with the first pricking (Mice 6 and 35); in other instances, however, it was necessary to prick the mouse a second time to induce long bleeding (Mice 11, 31, 43, and 44).

TABLE II

COMPARATIVE STUDIES OF DIFFERENT TESTS ON MICE WHICH RECEIVED 3,3′-METHYLENE-BIS-(4-HYDROXYCOUMARIN) ORALLY FOR THREE DAYS

GROUP	NUMBER OF MICE	MG./KG. DAILY	RANGE OF BLEEDING TIME (SECONDS)	RANGE OF COAGULATION TIME (SECONDS)	RANGE OF PROTHROMBIN TIME (SECONDS)	HEMATOMA	
						POSITIVE	NEGATIVE
1	7	10	25-152	45- 139			
2	7	20	29-127	70- 230			
3	6	40	52-184	44- 312			
4	1	60	> 900	417	D		1
5	3	60	480-870	211*	D	2	1
6	2	60	195-285	480- 870	127->180	1	1
7	1	60	64	58	42		1
8	8	60	60-232	85- 215	18- 24		8
9	1	80	> 900	D	D	1	
10	2	80	420-480	158- 165	24- 28	1	1
11	1	80	300	495	169		1
12	4	80	63-154	600-1590	149->180	2	2
13	4	80	60-180	125- 256	23- 32		4
14	4	80	38-110	362- 458	56-142		2
15	4	100	> 900	480-1500	> 180*	3	1
16	2	100	420-660	174- 301	30- 47		2
17	1	100	360	1200	> 180	1	
18	1	100	113	1860	140	1	
19	3	100	110-210	65- 180	22- 26	2	1

*Done on one mouse because the remaining mice in the group died.
D, Died.
Longest bleeding time value was taken if there was a disparity between duplicate tests.

Table II summarizes the effect of various doses of the hemorrhagic agent on the bleeding time, coagulation time, prothrombin time, and hematoma formation in 62 mice. Thirty-five mice which were treated with 10 to 100 mg. per kg. did not exhibit any changes in either the bleeding, coagulation, or the prothrombin times (Groups 1, 2, 3, 8, 13, and 19). Prolonged values in one or more tests occurred in the remaining 27 mice. Out of 43 mice which received from 60 to 100 mg. per kg., 15 mice had bleeding times longer than 300 seconds. Six mice given this treatment had bleeding times in excess of 900 seconds (Groups 4, 9, and 15). The

prothrombin time in these groups was in excess of three minutes. Two mice bled 300 and 360 seconds; they also had prolonged coagulation and prothrombin times (Groups 11 and 17). Three mice bled from 480 to 870 seconds (Group 5); one mouse which was tested had a normal coagulation time; the other two died soon after the bleeding time test, from blood loss. Two mice had prolonged bleeding time with normal coagulation and prothrombin times (Group 10). Two mice had prolonged bleeding time with normal coagulation time and slightly prolonged prothrombin time (Group 16). Eleven mice had normal bleeding time and markedly increased coagulation and prothrombin times (Groups 6, 12, 14, and 18). Only one mouse exhibited a prolonged prothrombin time, while the other tests were normal (Group 7). At autopsy 14 of the 41 mice which were examined had hematomas. Some animals had from one to several hematomas, varying in size from a few millimeters to one centimeter in diameter, usually just beneath the skin. They were found on the feet, legs, back, abdomen, neck, and ears. Out of 25 mice with prolonged bleeding or prothrombin times, 12 mice had hematomas. In the remaining 16 mice with normal prothrombin, coagulation, and bleeding times, two mice had hematomas.

DISCUSSION

The hemorrhagic agent, when given in adequate doses, will prolong the bleeding time in mice. The mechanism by which 3,3′-methylene-bis-(4-hydroxycoumarin) prolongs bleeding in mice is not understood at present. It is certain that heparin prolongs the coagulation of blood in a different way than the hemorrhagic agent, due to the immediate anticoagulant action of heparin in vivo and in vitro, and because it does not affect the prothrombin time. The hemorrhagic agent, on the other hand, increases both the coagulation and the prothrombin time in vivo. Link and associates[7] suggested, from dilution studies on normal and pathic rabbit plasmas, that the action of 3,3′-methylene-bis-(4-hydroxycoumarin) was not necessarily restricted to the prothrombin time mechanism. Even though we did not do dilution studies on mouse's heart blood, we believe that when our values were in excess of 30 seconds they were significantly prolonged.

It is difficult to offer an explanation for the lack of correlation between the bleeding time and the coagulation and prothrombin times in some of the animals. In those instances where the bleeding time was normal with prolonged coagulation and prothrombin times, long bleeding times might have followed one or more normal bleeding time values. We did not subject the animals to more than two bleeding time tests, since excessive blood loss could have affected the coagulation and prothrombin times, which were done after the bleeding time tests. Link and associates[7] observed whole plasma prothrombin times of approximately 10 minutes in dogs, and in excess of 250 seconds (12.5 per cent plasma) in rabbits and rats without any tendency to hemorrhage, following large doses of

3,3′-methylene-bis-(4-hydroxycoumarin). These findings demonstrate that the prothrombin time may not necessarily indicate a bleeding tendency. The phenomenon of prothrombin time is not well understood at present. One of us (A. L. C.) advanced the view that inactive thrombin, which is present in the circulating blood, plus a complementary factor constitute the prothrombin complex.[8] Prothrombin is only a precursor of thrombin in that in the heparin-prothrombin complex, preformed thrombin is inactivated by antithrombin which is composed of heparin and the complementary factor. Thromboplastin in the presence of calcium and the complementary factor has its neutralizing effect upon heparin, thus activating the thrombin. On this basis it was assumed that the prothrombin time expresses the speed with which the activation of thrombin occurs and the degree of concentration of the activated thrombin from the prothrombin complex. The prothrombin time, therefore, does not necessarily measure the prothrombin content.

It is quite possible that still another factor, probably present in the skin,[4] functions in the mechanism of hemostasis. Even though the skin (or tissue) factor is a hypothetical substance, we believe it may well play a role in either prolonged or normal bleeding in mice which receive the hemorrhagic agent. It may be that excessive amounts of the skin factor are present in mice with normal bleeding time and prolonged coagulation and prothrombin times. Likewise, decreased amounts of the skin factor may be present in mice with long bleeding time and normal coagulation and prothrombin times. Experiments in heparinized mice suggest that variable amounts of the skin factor are present.[4]

We found no petechiae in our mice during life or at autopsy; neither were we able to find any reference in the literature[2, 3] regarding petechiae in human beings after treatment with the hemorrhagic agent. We doubt that the hemorrhagic agent exerts a loosening effect on the cement substance of the capillary endothelial cells. Bingham, Meyer, and Pohle[3] reported that arteriolar, capillary, and venule dilatation occurred in dogs which received the hemorrhagic agent. It may well be that prolonged bleeding may follow dilatation of the smaller vessels; however, we feel that a more likely explanation for the prolonged bleeding is due to changes in the characteristics of the clot. We believe heparin and the hemorrhagic agent may delay the hemostasis which more adequately is measured by the clot resistance test[9-11] in vivo and the clot firmness test in vitro.[12]

The following method of clot resistance was used to determine the ability of the clot to resist increases in venous pressure in mice.[11] The venous bleeding time was determined after transversely cutting a vein in the middle portion of the mouse's tail with a stylet measuring 0.5 by 1.5 mm. In an attempt to renew bleeding, a cuff pressure of 75 mm. of Hg was applied proximal to the wound from 18 to 34 minutes after bleeding had stopped. Out of 109 normal mice this pressure provoked bleeding in 5.5 per cent, whereas in mice treated with the hemorrhagic agent for three

days bleeding was frequently initiated. These findings on clot resistance indicate that the hemorrhagic agent may prolong bleeding and impair both the firmness of the clot and its ability to adhere to the skin wound.

Hematomas were the only clinical manifestation effected by the hemorrhagic agent. In Group 8 negative tests corresponded with the absence of hematomas, although this was not the case in two animals in Group 19; we found hematomas even when the bleeding time, coagulation and prothrombin times were normal. They were not, on the other hand, always present when one or more tests exhibited abnormal values. It must be borne in mind that the origin of hematoma formation was not known. It may be assumed that the occurrence of a hematoma could be due to trauma in those animals which acquired a hemorrhagic tendency after treatment with 3,3′-methylene-bis-(4-hydroxycoumarin).

SUMMARY

1. A prothrombin time test was developed in mice, using 0.1 c.c. heart blood. Prothrombin time values ranged from 15 to 28 seconds and averaged 22.4 seconds.

2. Following oral administration of 60 to 100 mg. per kg. of 3,3′-methylene-bis-(4-hydroxycoumarin) over a period of three days, the bleeding time was prolonged in some of the mice.

3. Comparison of bleeding time with coagulation and prothrombin times showed a lack of correlation in many of the mice. Some animals had prolonged bleeding times with normal coagulation and prothrombin times, while others had prolonged coagulation and prothrombin times with a normal bleeding time.

4. Hematomas were more frequently found in mice with prolonged bleeding time or prothrombin time than in mice with normal values.

5. The relation of bleeding time and prothrombin time to hemorrhagic tendency was discussed. It appeared that still other factors which were discussed are involved in hemostasis.

We are indebted to Dr. Karl Paul Link who kindly sent to one of us (A. L. C.) his unpublished paper, which was helpful in the interpretation of our results.

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A NEW METHOD OF SKIN PROTECTION FOR ILEOSTOMIES AND COLOSTOMIES

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ONE of the most annoying complications following an ileostomy or colostomy is the irritation caused by the constant contact of the surrounding skin with the discharging fecal material. It is during the immediate postoperative period, before a suitable bag can be fitted because of edema of the stoma, that this complication is most likely to occur. The resultant maceration of the skin may become so extensive as to cause the patient more pain and discomfort than the original disease.

We have attempted to prevent this condition by utilizing the various ointments (zinc oxide, vaseline, aluminum paste, etc.) recommended in standard texts but have not had much success. The diarrhea that occurs even with the use of a proper diet and constipating medication washes away the ointment in a short time and exposes the skin to the irritating action of the stool. Even with a more solid stool, the admixture of the ointment and fecal material directly on the skin makes the changing of dressings a slovenly procedure for the nurse and an unpleasant one for the patient.

Following the suggestion of DeBakey and associates,[1] we tried using a solution of vinylite resin* for this purpose but found that this also could not withstand the continual washing effect of the fecal material. However, on mixing collodion with the vinylite resin an excellent, thick, impermeable transparent film is obtained which is easy to apply and adheres closely to the skin. Since we have been using this solution, the absence of skin irritation in all types of enterostomies has been striking and a source of gratification to both patient and surgeon.

The formula used is as follows:

Vinylite resin	25 Gm.
Acetone	100 c.c.
Collodion	25 c.c.

DIRECTIONS FOR USE

1. The first application of the solution is best done immediately prior to opening the enterostomy.

2. Any ointment which is present is completely removed and all of the skin area completely cleansed with ether and acetone.

*This material was supplied through the courtesy of the Carbon and Carbide Chemicals Corporation, Chicago, Ill.

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3. The solution is poured on the skin around the incision and smeared evenly with an applicator or tongue depressor. The sides of the exteriorized bowel may be covered with the solution without any harmful effect.

4. At least ten to twenty minutes must be allowed for thorough drying of the solution and the formation of an adequate film.

5. The bowel is then opened and a dry sterile dressing applied.

6. The solution is reapplied without removing the previous coats as often as necessary depending upon the consistency and amount of the fecal drainage. This may vary from several times daily to once every few days.

The solution may also be used to advantage for protection of the skin in cases of fecal fistulas and profusely draining infected wounds.

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Recent Advances in Surgery

CONDUCTED BY ALFRED BLALOCK, M.D.

PRINCIPLES IN THE PROTECTION OF PATIENTS WHO RECEIVE BLOOD

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DURING the past ten years there has been a marked increase in the number of blood transfusions in almost all hospitals, since indications for their use have become more generally and clearly understood. This is particularly true in surgery. The value of blood therapy in controlling fluid balance, in nutrition, in the treatment of traumatic and thermal shock, in hemorrhage, in infection, and in wound healing is much better known and is becoming still more widely recognized.

Most surgeons show little interest in and lack knowledge of the careful laboratory work necessary before blood can be given safely in transfusion. The laboratory is too often considered a remote agency entrusted with a trivial routine responsibility, that of grouping and matching blood prior to transfusion. Moreover, the surgeon is inclined to give uncritical acceptance to those methods in use in the hospital. Yet in the smaller hospitals the responsibility for selection of blood usually falls to a house doctor, who was exposed to the theories and technique of grouping and matching for one morning during the sophomore year of his medical school training, and in the larger hospitals to a technician burdened with too many duties to give special thought to one problem.

Details of preoperative preparation, operative procedure and technique, and postoperative management, including nursing care, are subjected to critical supervision by the attending surgeon. Yet all these efforts to apply the best known standards of safety may be and frequently are neutralized, either by delay as a result of uncertainty in the laboratory or by an error which precipitates a hemolytic transfusion accident. Just seven years ago at the Cincinnati General Hospital a young woman came to thoracoplasty after sanatorium management had proved to be inadequate. She received careful preoperative preparation, good anesthesia, and excellent surgery. She died during her first postoperative day shortly after receiving 300 c.c. of incompatible blood in transfusion. Recheck of the grouping and direct match tests showed agglutination of the donor cells at the end of one hour by both the anti-A test serum and the recipient's serum. This was not detectable at the end of one-half hour. The methods and materials which had been provided and

which had proved adequate for the usual blood specimen had been accepted uncritically by the surgical house officer responsible for the laboratory work.

Since that time I have been intimately connected with the laboratory aspect of blood transfusion. As volunteer director of the Red Cross Blood Transfusion Service which was developed in the department of surgery of the University of Cincinnati and which serves the entire Cincinnati area, I have had an opportunity to encounter many problems at the Cincinnati General Hospital and fourteen other hospitals, concerning the grouping and matching of blood. It becomes of importance to relate some of the pitfalls which have come to my attention so frequently that I cannot help but believe that proper standards of safety are frequently ignored.

The purpose of this article is to draw the attention of clinicians to the causes of frequent accidents and delays which for the most part could be avoided.

As a result of our experience with a carefully supervised series of more than 12,000 blood transfusions given during four years we have concluded that the vast majority of transfusion accidents and delays are due to a lack of knowledge and application of the following principles.

1. *The Use of Test Serums of High Titer.*—The titer of a and b agglutinins and A and B agglutinogens in the blood of individuals is known to vary widely. Despite this, it is common practice in many hospitals to select group A and group B individuals as donors for test serums merely because the agglutinating effect of their serums on one or two specimens of anticells appears to be quite pronounced. Test serums selected in this manner may fail or offer poorly defined criteria of agglutination when placed with A or B cells with less pronounced agglutinogen activity. Borderline criteria of agglutination may result in errors in grouping or delay in providing blood due to uncertainty in the laboratory. During the past year two cases have come to our attention in which donors of subgroup A_2 were grouped as O for this reason. In each case the group A blood was given to a group O recipient, resulting in death of the recipient.

Unfortunately, reliance cannot always be placed upon the agglutinin titer of commercially prepared test serums. All test serums to be used, whether prepared in the hospital or in the commercial laboratory, should be selected because of superlative agglutinin titer. Determinations may be made by the use of the Coca[1] method of slide titration or by the method of serial titration.[2] Definitions of safe titers have been made repeatedly[3] but very few laboratory technicians know the titer of the test serums which are in current use in their own laboratories.

2. *Failure to Observe a Well-Known Principle of Agglutination.*—It is a very common practice to select a group O donor for a group AB recipient if a member of the latter blood group is not available. The

principle of dilution is relied upon to inactivate incompatible a and b agglutinins in the donor's serum. In the past year one case has come to our attention in which this factor resulted in death because the a agglutinin in the serum of the donor was of unusually high titer. Similar cases are reported in the literature. If group A donors are selected for group AB individuals, only one incompatible antigen-antibody complex is present and its potency may be determined easily by the use of a simple quantitative direct match test.

3. *Close Observation of the Patient During Transfusion.*—With the advent of blood banks and the increased requirement, blood transfusion has become very commonplace and informal. In many instances the transfusion is begun and a busy intern feels it necessary to leave in order to accomplish other work. Unfortunately, mistakes in grouping and matching of blood and confusion of specimens in the laboratory do occur. This is particularly true where blood banks are in operation, despite careful regulation, and may result in transfusion of incompatible blood. Early symptoms may not appear in a hemolytic transfusion reaction, but they frequently do, and the interruption of the transfusion by the attending physician may be lifesaving. Two cases which occurred at the Cincinnati General Hospital are in striking contrast and serve to illustrate the importance of close early observation.

No. 1.—A group A blood was given to a patient belonging to group O. Seventy-five cubic centimeters were given when the patient complained of paresthesia in the extremities and precordial pain and the transfusion was interrupted. Later oliguria, hemoglobinuria and uremia and laboratory recheck established the diagnosis of a hemolytic transfusion reaction. The patient recovered.

No. 2.—A group A blood was given to a patient belonging to group B, due to confusion of specimens. The transfusion was begun and the patient was not observed by a physician throughout. He received 500 c.c. of incompatible blood. Anuria and death due to uremia followed.

Although there are many factors contributing to the severity of a reaction other than the amount of incompatible blood which a patient receives, it is reasonable to believe that interruption of a blood transfusion after only a few cubic centimeters of incompatible blood have been given affords more chance for recovery. If early mild subjective complaints or objective signs are to be regarded as contraindications for continuing transfusion, it is difficult to condone any practice wherein a physician is not observing the patient carefully.

4. *Delays in the Laboratory Due to False Agglutination Being Interpreted as True Agglutination.*—Almost every week a case comes to our attention in which donor after donor of the same blood group as the patient is rejected by a laboratory because false agglutination is interpreted as true agglutination in the direct match test. The causative factors of this phenomenon are almost always attached to the blood of the patient and numerous samples of compatible blood are rejected.

If the blood is needed urgently, this confusion becomes hazardous. Increased time and expense affect the laboratory.

We have observed many such situations and they arise most frequently in the following circumstances: 1. Occasional effect of sulfonamide blood concentration; 2. sepsis with high sedimentation rates; 3. severe hemorrhage and other extreme anemias; 4. leucemia; 5. cold agglutinations due to the use of icebox samples in the test.

False agglutination due to these conditions can be promptly distinguished from true agglutination in practically all cases by the use of the following laboratory principles. First, by performing the direct match test with an open technique on a slide and stirring to break up the clumps under the microscope. In true agglutination agitation by stirring produces more marked agglutination. If specimens on a slide are placed under moist Petri dishes, this technique is possible. Sealed cover slip preparations for compatibility tests make it impossible. Second, microscopic examination of the patient's blood diluted in saline solution will in the above situation show the same false agglutination effect.

5. *Performance of Compatibility Tests Before All Transfusions, Even Though the Blood Is of the Same Group.*—Recently a case came to our attention in which a recipient of blood group A_2B was given two transfusions of group B blood because AB blood was not available. Twenty-four hours later a succeeding compatibility test with group AB blood showed incompatibility. This was presumably due to an accumulation of anti-A antibodies of sufficient potency to agglutinate the A cells in the blood which was being tested.

In some hospitals compatibility tests are not performed, reliance being placed wholly upon the grouping and the transfusion of like groups. The known existence of rare atypical agglutinins and the possibility of the ever present human factor of error in determining blood groups make it necessary that compatibility tests be performed in order to safeguard the patient receiving blood.

6. *The Use of Rh– Donors.*—Recently unquestionable evidence that hemolytic transfusion reactions occasionally may be caused by incompatible Rh factors has been produced.[4] Routine tests to distinguish Rh+ from Rh– red cells are impracticable at present because of the extreme difficulty in providing anti-Rh serums in amounts that would be required. It is possible for the hospital laboratory to secure a small amount of anti-Rh serum and to maintain a list of Rh– donors. It is also possible to perform modified direct match tests for anti-Rh factors.[5] These should be reserved for use (1) for patients who are or who have been recently pregnant, (2) for patients who are receiving multiple transfusions over periods of days, and (3) for the newborn with erythroblastosis fetalis.

SUMMARY AND CONCLUSIONS

The difficulties in blood transfusion outlined above are more common than is generally supposed and most of them can be corrected by better observance of the known standards of safety. This requires (1) the use of test serums of highest titer, (2) a more popular knowledge and application of the established principles of hemagglutination, and (3), close observation of the patient during transfusion as added insurance against laboratory error.

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Book Reviews

Ophthalmology and Otolaryngology. A manual prepared and edited by the Subcommittee on Ophthalmology and Otolaryngology of the Committee on Surgery of the Division of Medical Sciences of the National Research Council. Harry S. Gradle, Chairman of Ophthalmology; Harris P. Mosher, Chairman for Otolaryngology. Volume II, Military Surgical Manuals. Pp. 331, with 126 illustrations. Philadelphia and London, 1942, W. B. Saunders Company. Cloth. $4.00.

This is the second volume in the series of six volumes comprising twelve military surgical manuals which are being developed under the auspices of the Division of Medical Sciences of the National Research Council. These manuals are to furnish the Medical Departments of the United States Army and Navy with a digest of necessary information in the field of military surgery. Most of the manuals deal with highly specialized surgical subjects. The digest of present-day information is to help the Army or Navy surgeon to apply skill when the necessity arises, to a field which may not be his own.

This volume gives approximately equal space to ophthalmology and to otolaryngology. The eight chapters on ophthalmology are contributed by five well-known oculists. The subject matter deals with functional testing, examination of the eye, acute visual disturbances, acute inflammations, injuries, medical treatment, local anesthesia about the orbit, and surgical procedures.

The section on otolaryngology is divided into seventeen chapters contributed by twelve otolaryngologists of note. A variety of subjects are discussed: primary treatment of gunshot wounds of the face, the ear in general, fractures of the temporal bone and of the cribriform plate, injuries to the labyrinth and labyrinthine function, group testing of hearing, malingering, roentgenologic diagnosis of petrositis, the ear in military aviation, re-education of the deafened soldier, re-education for speech defects, the nose and throat in general, paralysis in connection with wounds in the throat, infections of the throat, chemotherapy, injuries of the esophagus, and injuries of the larynx, hyoid bone, and trachea.

This small manual seems to fulfill the purpose for which it is intended, a brief digest of up-to-date information on the ophthalmologic and otolaryngologic problems of the military surgeon, not the specialist in these fields, but the nonspecialist.

War Medicine. A Symposium edited by W. S. Pugh, Commander, U. S. N., for the Philosophical Library. Pp. 565, illustrations, 76. New York, 1942, F. Hubner and Company, Inc.

This volume represents a symposium of articles dealing with medical military subjects, as selected from the current medical journals of America and Britain. Under the editorship of W. S. Pugh, Commander, U. S. N., retired, fifty-seven articles have been chosen for inclusion in the book, and have been arranged in three sections, namely, Surgery, Aviation and Naval Medicine, and General Medicine. The subjects or articles selected represent a splendid variety of subjects which would be of vital interest to medical officers on duty.

Naturally, in a symposium of this type there can be no correlation of material such as would be achieved by one author. Moreover, since the material is presumably not edited from the standpoint of scientific statements, numerous errors

or contradicting statements are encountered. Although the article dealing with burns, beginning with page 41, correctly emphasizes the necessity of débridement, on page 21 in a paragraph dealing with burns, is a statement, "no attempt at surgical cleaning is made"; this latter statement is erroneous, and is contradictory to those in the article on burns beginning on page 41. On page 22, the maximum limit of 40 Gm. sulfanilamide for a patient would appear to be needlessly high. The reviewer was surprised to see at the bottom of page 144, the statement that a four-tail bandage "will also give some temporary support to a fracture of the mandible"; in his experience such a dressing exerts too much backward displacement, thereby tending to obstruct the pharyngeal airway.

The authors quote too freely from experiences in World War I. The chapter on burns, however, is one of many exceptions to this criticism; it thoroughly discusses the tannic acid and triple-dye methods along with other procedures as practiced in Britain during this war. Unfortunately, this material and the book were apparently assembled a few weeks or months too early to allow inclusion of the pressure dressing method of Koch and Reid.

Although the section on Surgery is not up to the standard of the other two sections, the articles on "Gunshot Wounds of the Heart," "Blast Concussion," "Blood Substitutes" and "Drainage of the Pleura" are splendid contributions. The article on "War Wounds and Compound Fractures" contains a splendid historical review of Lister's principles of asepsis, and the proper emphasis on the importance of immobilization in the treatment of wounds as well as fractures.

Considering how meager is our knowledge of aviation medicine, the section dealing with this subject is remarkably informative and well written. With the information contained in these articles alone a flight surgeon could obtain a good insight into the proper care of pilots, and treatment of symptoms derived from the hazards of centrifugal force and changes in altitude.

Altogether the book is very informative and interesting. Although it cannot be used as a text because it is deficient in various subjects, it nevertheless would be of inestimable value as an addition to a medical military library.

Anatomy of the Hand; The Principles of Anatomy as Seen in the Hand. By Frederic Wood Jones, D.Sc., F.R.S., F.R.C.S., University of Manchester, England. Ed. 2. Pp. 407, with 144 illustrations. Baltimore, 1942, Williams & Wilkins Company. $7.50.

This book was prepared during the 1914 War as a guide for a series of lectures in applied anatomy as a part of the course of instruction to officers of the R. A. M. C. The first edition was published in 1920.

Written by the professor of anatomy at the University of Manchester, the material is authoritatively presented. The second edition has been revised, and six new chapters and twenty new figures have been added. The author's interesting style and practical descriptions should make the subject matter attractive to professional groups in the related medical sciences.

The first fourteen chapters contain an interest for comparative anatomists, while the surgical interest is attracted to the succeeding ten concise chapters, devoted to the practical anatomy of the fascias, bones, joints, muscles, tendons, and tendon sheaths of the hand. The remaining nine chapters are devoted to discussions on the functions of the hand, the motor and sensory pathways, the nerves, the vascular channels, and lymphatics.

This book will be of interest to the student of anatomy, and especially the busy medical officer of the R. A. M. C., for whom it is primarily intended.

Sulfanilamide and Related Compounds in General Practice. By Wesley W. Spink, M.D., F.A.C.P. Pp. 374, with charts and table. Chicago, 1942, Year-Book Publishers, Inc. $3.

This book has been greatly increased in size and comprehensiveness. In a field which is advancing and changing as fast as any in medicine, and in which the amount of published material is almost overwhelming, this little book constitutes an admirable condensation of the present knowledge of the subject and will serve as an up-to-date and authentic guide and summary for the surgeon as well as for the medical man. Few are the professional men today who can afford to do without this excellent monograph.

The Principles of Neurological Surgery. By Loyal Davis, M.S., M.D., Ph.D. Ed. 2. Pp. 503, with 298 illustrations. Philadelphia, 1942, Lea & Febiger. $7.

This is a much improved second edition of a neurosurgery text, the first edition of which was published in 1936.

Some of the material has been rewritten and rearranged. The chapters are much better subdivided by subchapter headings; for example, Chapter IV, Intracranial Abscess, which had no subdivisions in the first edition, is now subdivided into Etiology and Pathogenesis, Pathology, Symptoms, and Surgical Treatment. Some new sections are added, such as electro-encephalography, arachnoiditis, tuberculosis of the skull, herniation of intervertebral disc, and others. The illustrations have been rearranged, many new ones added, and some of those in the first edition deleted. All of these improvements and additions have increased the book size from 416 pages to 494 pages.

This is the only available textbook of neurosurgery and, therefore, is the only place where all of this material is collected together. It is recommended to the general practitioner and others who occasionally need some information concerning the more common neurosurgical problems.

Urological Diseases of Pregnancy. By E. G. Crabtree (with a chapter by G. C. Prather). Pp. 472, with 158 illustrations. Boston, 1942, Little, Brown & Company.

The problems relating to the urinary tract in pregnancy have been pretty well covered, a little at a time, by a great number of authors in widely scattered books and periodicals, but this work is the first to come to the attention of the reviewer, in which the pertinent data are assembled, together with a very extensive bibliography. Its value is, of course, enhanced by the extensive personal experience of the author at the Boston Lying-In Hospital and in private practice.

There are fairly extensive discussions of the effects of pregnancy upon the body and upon its economy in general, as well as upon the urinary tract itself. There are chapters comparing the effects of pregnancy in lower animals with those in the human being as well as with the effects of tumors other than the pregnant uterus upon the urinary tract. The work is of particular practical value to the urologist and general practitioner because of its discussions of special problems which, while they may be commonplace to the busy obstetrician, are puzzling to the physician who encounters them only occasionally. I refer to the situations created by pyelonephritis, atony of the bladder, tuberculosis of the urinary tract, stones, solitary kidneys, renal neoplasms, and the like. The techniques of examination and modes of treatment are well covered, as is the relationship of the toxemia of pregnancy to the urinary tract.

Of interest to nearly all practitioners are the chapters on the oliguria of transfusion reactions, and the untoward effects of the sulfonamides on the urinary tract.

The critical reviewer can, of course, find points which arouse him, although they are minor ones, as the very frequent use of "scarification" to mean cicatrization or, more simply, scarring and of "physiology" for function, as well as "etiology" for cause. The last two are, of course, attributable to the widespread, if deplorable, use of medical slang.

One regrets that the discussions of the cause of hydronephrosis in pregnancy, and of the effect of tumors of the female pelvis upon the kidneys are treated so briefly, and one shudders at the author's failure to discuss the value of nasal suction (Wangensteen and Paine) in ileus, the more so because the author mentions the high mortality of the condition.

The book is warmly recommended to urologists, obstetricians, and general practitioners, and should be a valuable source of references for investigators in the fields concerned.

First Aid, Surgical and Medical: An Advanced Guide. By Warren H. Cole, M.D., F.A.C.S., and Charles B. Puestow, M.D., Ph.D., F.A.C.S., University of Illinois, Ed. 1. Pp. 351, illustrations 92. New York, 1942, D. Appleton-Century Company, Inc.

At a time when the war has caused large numbers of civilians to be trained in the essentials of first aid, an authoritative and yet elementary textbook is of first importance. This readable book fulfills this need admirably.

An excellent introduction precedes the descriptions of procedures for specific injuries, and although it is verbose in places, it nevertheless offers an excellent background of knowledge for the first-aid worker. There are sections on each of the types of conditions to be encountered in either civil or military life, such as shock, lacerated wounds, fractures, burns, gas and bomb injuries, etc.

There are some points in the book with which most physicians would take issue, such as several of the types of bandages described, yet the vast bulk of the material is accurate, correct, and well expressed. This book is not for beginners, as the title indicates, but those who have had a rudimentary first-aid course will find it of inestimable value in achieving a further understanding of the subject.

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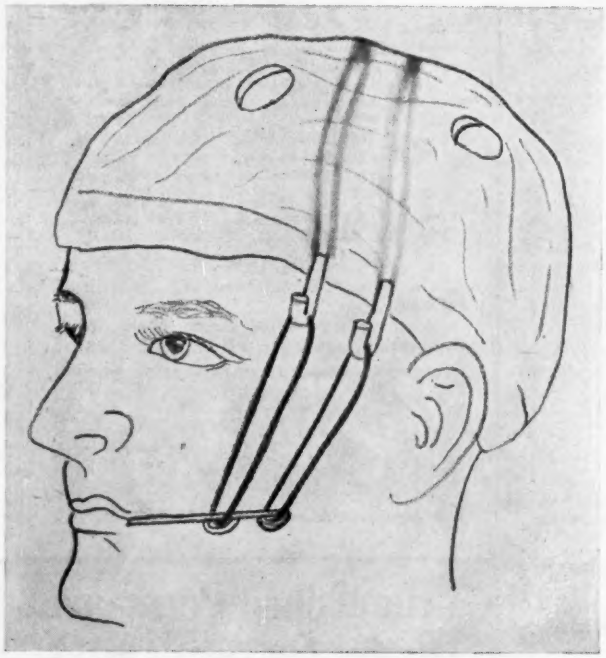

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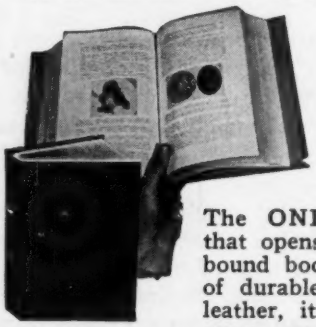

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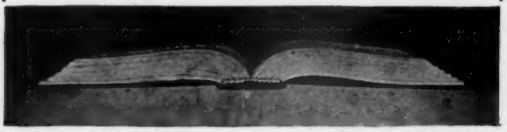

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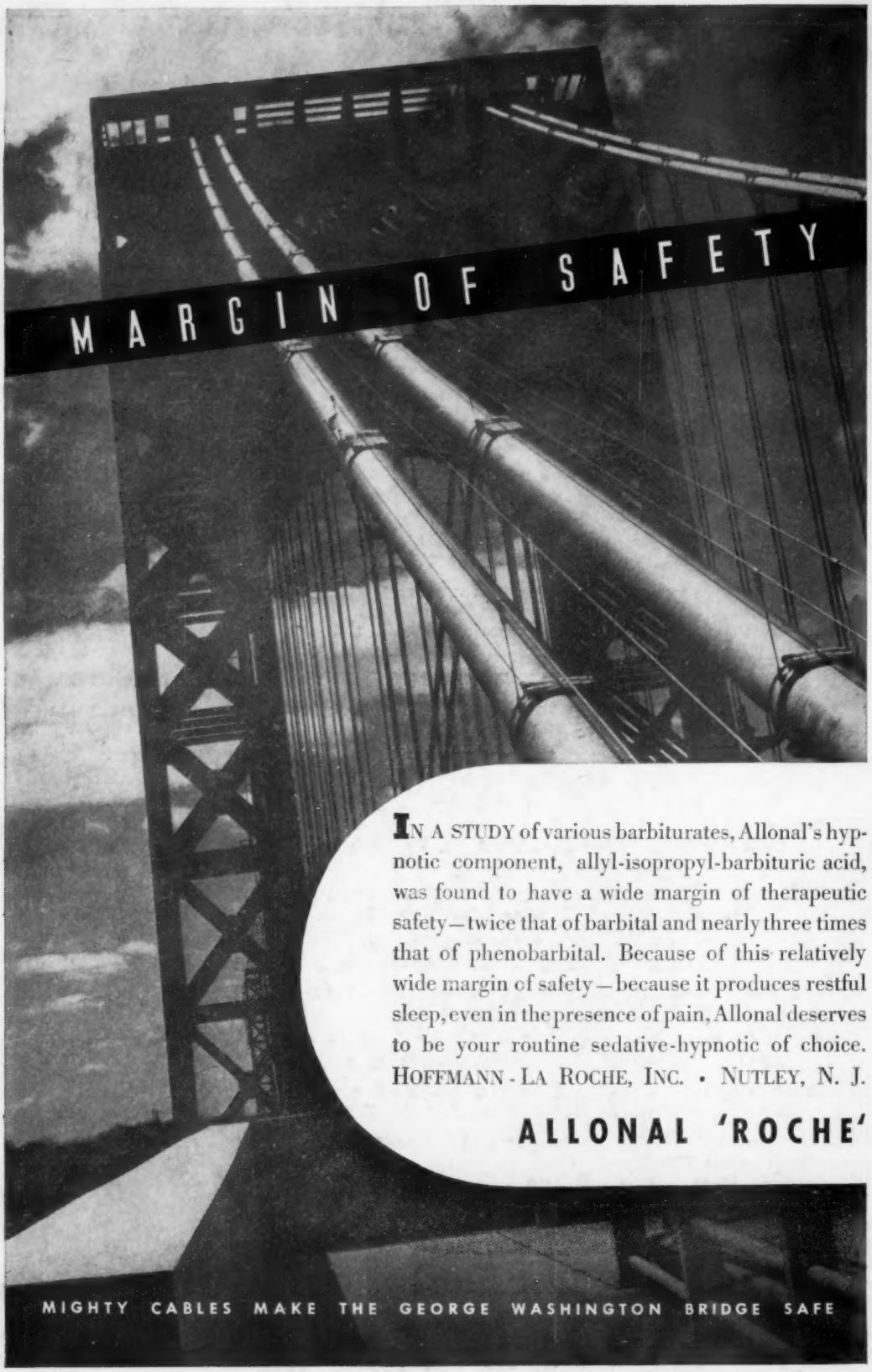

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